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(54) **THERAPEUTIC COMPOSITIONS AND METHODS**

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(57) **ABSTRACT**

The present application provides novel binding proteins, including human binding proteins that specifically bind to the human ErbB2.

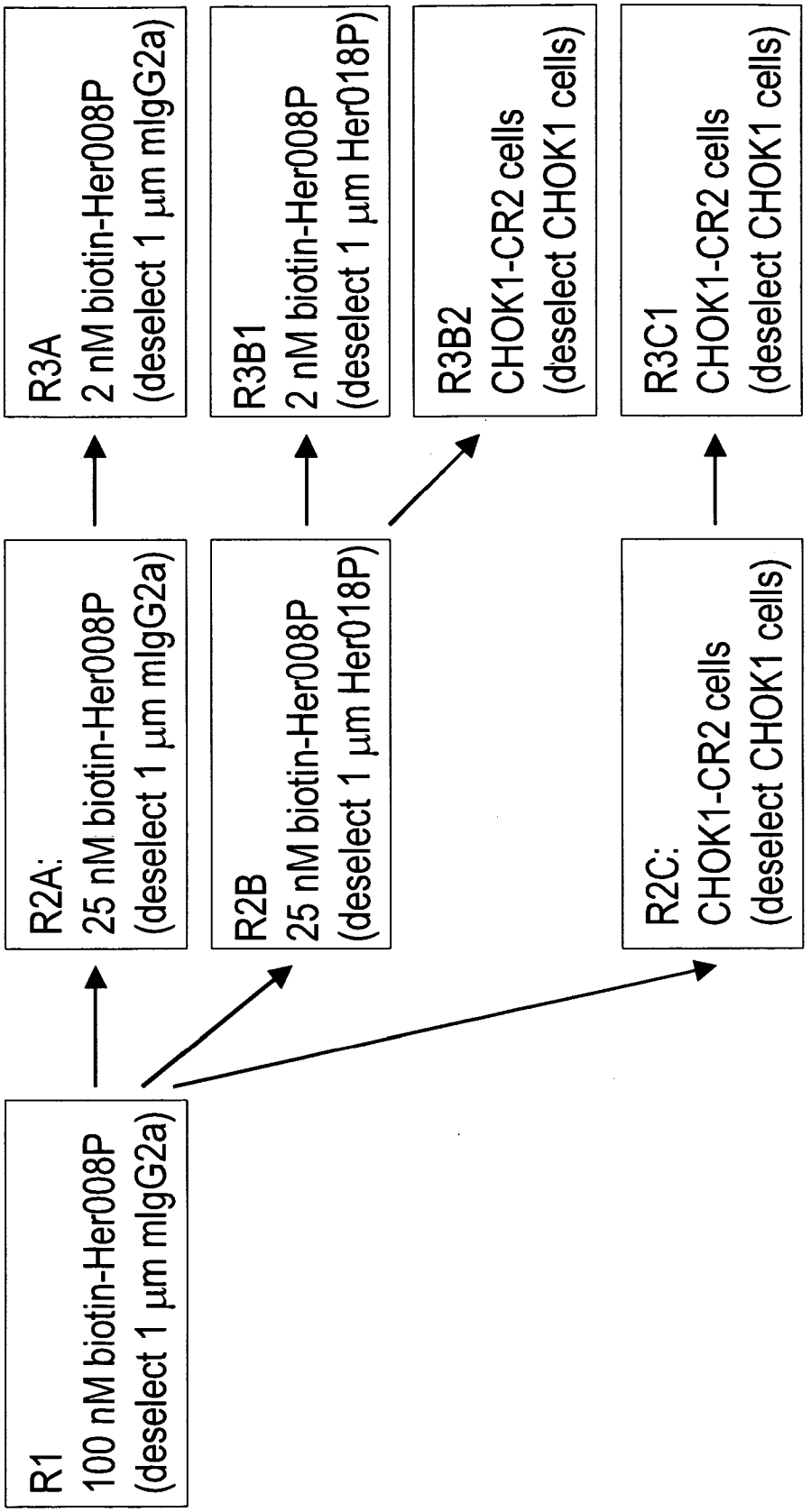

R1
100 nM biotin-Her008P
(deselect 1 µm mIgG2a)
R2A:
25 nM biotin-Her008P
(deselect 1 µm mIgG2a)
R2B
25 nM biotin-Her008P
(deselect 1 µm Her018P)
R2C:
CHOK1-CR2 cells
(deselect CHOK1 cells)
R3A
2 nM biotin-Her008P
(deselect 1 µm mIgG2a)
R3B1
2 nM biotin-Her008P
(deselect 1 µm Her018P)
R3B2
CHOK1-CR2 cells
(deselect CHOK1 cells)
R3C1
CHOK1-CR2 cells
(deselect CHOK1 cells)

Figure 1

```
                    FW 1                    CDR 1          FW 2                CDR 2
VH1_DP14            QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYGIS----WVRQAPGQGLEWMGWISA-----YNGNTNYAQKLQG
S1R3B2_BMV_1G2      QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYGIS----WVRQAPGQGLEWMGWISA-----YNGNTNYAQKLQG
S1R3B1_BMV_1A1      EVQLVQSGAEVKEPGASVKVSCKASGYDFSNYGFS----WVRQAPGQGLEWMGWISS-----YNGYTNYAQRLQG

                    FW 3                                    CDR 3                FW 4
VH1_DP14            RVTMTTDTSTSTAYMELRSL--RSDDTAVYYCAR.....................................
S1R3B2_BMV_1G2      RVTMTTDTSTSTAYMELRSL--RSDDTAVYYCARVPGVSGSYPDYYYM---------DVWGKGTLVTVSS.
S1R3B1_BMV_1A1      RVTMTTDTSTSTAYMELRSL--RSDDTAVYYCARDRGLGNWYF--------------DLWGQGTLVTVSS.
```

Figure 2A

```
                    FW 1                    CDR 1          FW 2                CDR 2
VH1_DP25            QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYAMH----WVRQAPGQRLEWMGWINA-----GNGNTKYSQKFQG
S1R3A1_BMV_1G4      QVQLVESGAEVKKPGASVKVSCKASGYTFTSYDIN----WVRQAPGQRLEWMGWINA-----GNGNTKYSQKFQG

                    FW 3                                    CDR 3                FW 4
VH1_DP25            RVTITRDTSASTAYMELSSL--RSEDTAVYYCAR.....................................
S1R3A1_BMV_1G4      RVTITRDTSASTAYMELRSL--RSDDTAVYYCARGRSYGHPYYF-------------DYWGQGTLVTVSS.
```

Figure 2B

```
                        FW 1                    CDR 1        FW 2                CDR 2
VH3_DP47                EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS----WVRQAPGKGLEWVSAISG-----SGGSTYYADSVKG
S1R3B2_DP47_1C9         EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS----WVRQAPGKGLEWVSAISG-----SGGSTYYADSVKG
S1R3C1_DP47_1H1         EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS----WVRQAPGKGLEWVSAISG-----SGGSTYYADSVKG
S1R3B2_DP47_1E8         EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS----WVRQAPGKGLEWVSAISG-----SGGSTYYADSVKG
S1R3B2_DP47_1E10        EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS----WVRQAPGKGLEWVSAISG-----SGGSTYYADSVKG
S1R3B1_DP47_1E1         EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS----WVRQAPGKGLEWVSAISG-----SGGSTYYADSVKG
S1R3A1_DP47_1A6         EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS----WVRQAPGKGLEWVSAISG-----SGGSTYYADSVKG
S1R3B1_BMV_1G11         QVQLVQSGGGLVQPGGSLRLSCAASGFTFSTYAMS----WARQAPGKGLEWVSSISG-----DGGRILDADSAKG

                        FW 3                                CDR 3                FW 4
VH3_DP47                RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCAK.....................................
S1R3B2_DP47_1C9         RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCARWRPLLDYHF--------------DQWGQGTMVTVSS.
S1R3C1_DP47_1H1         RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCARVSGSHFPFF-------------DSWGQGTMVTVSS.
S1R3B2_DP47_1E8         RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCARQSGADWYF---------------DLWGRGTLVTVSS.
S1R3B2_DP47_1E10        RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCARGYSGYDDP---------------DSWGRGTTVTVSS.
S1R3B1_DP47_1E1         RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCARGGSGS-----------------DYWGQGTMVTVSS.
S1R3A1_DP47_1A6         RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCARDLGIDPLWSGYYTPL--------DYWGRGTMVTVSS.
S1R3B1_BMV_1G11         RFTISRDNSKNTLYLQMNGL--RVEDTALYYCARADG--------------------NYWGRGTMVTVSS.
```

Figure 2C

```
                        FW 1                    CDR 1        FW 2                CDR 2
VH3_DP47                EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS----WVRQAPGKGLEWVSAISG-----SGGSTYYADSVKG
S1R3C1_BMV_1H11         GVQLVESGGGLVKPGGSLRLSCAASGFTFSSYNMN----WVRQAPGKGLEWVSAISG-----SGGSTYYADSVTG

                        FW 3                                CDR 3                FW 4
VH3_DP47                RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCAK.....................................
S1R3C1_BMV_1H11         RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCAKDTSGWYGDGM-------------DVWGRGTLVTVSS.
```

Figure 2D

```
1_VH_Her2_S1_pileup_17843.txt  MSF: 124  Type: P  May 21, 2007 16:01  Check: 413 ..

 Name: 1_VH_Her2_S1R2A_CS_1D11  Len:   124  Check: 7283  Weight:  1.00
 Name: 1_VH_Her2_S1R2C_CS_1D3  Len:   124  Check: 7153  Weight:  1.00
 Name: 1_VH_Her2_S1R3C1_CS_1B10  Len:   124  Check: 5945  Weight:  1.00
 Name: VH1_DP10_germline  Len:   124  Check:   32  Weight:  1.00

//
                1                                                    50
1_VH_Her2_S1    EVQLVQSGSE VRRPGSSVRV SCTASGDTSS SFTVNWLRQA PGQGLEWMGG
1_VH_Her2_S1    QVQLVQSGSE VRRPGSSVRI SCTASGDTSS SFTVNWVRQA PGQGLEWMGG
1_VH_Her2_S1    QVQLQQSGAE VKKPGSSVKV SCKASGGTIS NYAISWVRLA PGQGLEWMGS
VH1_DP10_ger    QVQLVQSGAE VKKPGSSVKV SCKASGGTFS SYAISWVRQA PGQGLEWMGG

                51                                                  100
1_VH_Her2_S1    ITPMFGTANY AQMFEDRVTI TADE...... MELSGLTSED TAVYFCATGP
1_VH_Her2_S1    ITPMFGTANY AQVFEDRVTI IADE...... MELSGLTSED TAVYFCATGP
1_VH_Her2_S1    IVPLHGTTNF AQKFQGRVTI TADESTSTSY MEVNVLTYED TAMYYCASLN
VH1_DP10_ger    IIPIFGTANY AQKFQGRVTI TADESTSTAY MELSSLRSED TAVYYCAR~~

                101                    124
1_VH_Her2_S1    SDYVWGSYRF LDTWGRGTTV TVSS
1_VH_Her2_S1    SDYVWGSYRF LDRWGRGTLV TVSS
1_VH_Her2_S1    WGY....... ...WGRGTLV TVSS
VH1_DP10_ger    ~~~~~~~~~~ ~~~~~~~~~~ ~~~~
```

Figure 2E

```
                    FW 1                    CDR 1          FW 2                CDR 2
VH6_DP74            QVQLQQSGPGLVKPSQTLSLTCAISGDSVSSNSAAWN--WIRQSPSRGLEWLGRTYYR----SKWYNDYAVSVKS
S1R3C1_CS_1D3       QVQLQESGPGLVKPSQTLSLTCGISGDSVSSNSAAWN--WIRQSPTRGLEWLGRTYYRS---SWYHNYAPSMNSR

                    FW 3                                   CDR 3                FW 4
VH6_DP74            RITINPDTSKNQFSLQLNSV--TPEDTAVYYCAR.....................................
S1R3C1_CS_1D3       LTIIADTSKNQFSLQLNSV---TPEDTAVYYCASGWAF-------------------DVWGRGTLVTVSS.
```

Figure 2F

```
                    FW 1                    CDR 1          FW 2                CDR 2
VH5_DP73            EVQLVQSGAEVKKPGESLKISCKGSGYSFTSYWIG----WVRQMPGKGLEWMGIIYP-----GDSDTRYSPSFQG
S1R3C1_CS_1A6       EVQLVQSGAEVKKPGESLKISCKGFGYNFRSAWIG----WVRQMPGKGLEWMGVIYP-----GDSDVRYSPSFQG
S1R3A1_CS_1B9       KVQLVQSGTEVKKPGESLKISCQGSGYRFSSDWIA----WVRQMPGKGLEWMGIVYP-----GDSDTRYSPSFQG
S1R3A1_CS_1D11      EVQLVQSGAEVKKPGESLKISCKGSGYTFTNHWIA----WVRQMPGKGLEWMGIIYP-----GDSETRYSPSFQG

                    FW 3                                   CDR 3                FW 4
VH5_DP73            QVTISADKSISTAYLQWSSL--KASDTAMYYCAR.....................................
S1R3C1_CS_1A6       QVTISADKSISTAYLQWSSL--KASDTAMYYCTRPVGQWVDS---------------DYWGKGTLVTVSS.
S1R3A1_CS_1B9       QVTISADKSISTAYLQWSGL--KASDTAKYYCARVQQAVGAKGYAM-----------DVWGKGTLVTVSS.
S1R3A1_CS_1D11      HVTISADKSISTAYLQWSTL--KDSDSAMYFCVRQARGWDDGRAGYYYSGM------DAWGQGTLVTVSS.
```

Figure 2G

	FW 1	CDR 1	FW 2	CDR 2
VH4_DP70	QVQLQESGPGLVKPSGTLSLTCAVSGGSIS	SSNWWS	---WVRQPPGKGLEWIG	EIY------HSGSTNYNPSLKS
S1R3B1_BMV_1H9	QVQLQESGAGLVKPSGTLSLTCAVSGGSIS	SGNWWS	---WVRQPPGKGLEWIG	EIS------HSGSTNYNPSLKS

	FW 3	CDR 3	FW 4
VH4_DP70	RVTISVDKSKNQFSLKLSSV--TAADTAVYYCAR	.....	
S1R3B1_BMV_1H9	RVTISVDKSKNQFSLNLSSV--TAADTAVYYCAR	VRGTVGDTRGP----------	DYWGQGTLVTVSS.

Figure 2H

	FW 1	CDR 1	FW 2	CDR 2
VH3_DP77	EVQLVESGGGLVKPGGSLRLSCAASGFTFS	SYSMN	----WVRQAPGKGLEWVS	SISS-----SSSYIYYADSVKG
S1R3A1_BMV_1F3	EVQLVESGEGLVKPGGSLRLSCTASGFTFR	SYSLN	----WVRQAPGQGLEWVS	SISS-----TSTYIYYADSVKG

	FW 3	CDR 3	FW 4
VH3_DP77	RFTISRDNAKNSLYLQMNSL--RAEDTAVYYCAR	.....	
S1R3A1_BMV_1F3	RFTISRDDAKNTLYLQMNSL--RAEDTAAYYCVR	LGSGGGYFP----------	DYWGRGTLVTVSS.

Figure 2I

```
                    FW 1                    CDR 1        FW 2                CDR 2
VH3_DP51        EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYSMN----WVRQAPGKGLEWVSYISS-----SSSTIYYADSVKG
S1R2C_CS_1H12   EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYGMN----WVRQAPGKGLEWVSYISS-----SGNTIFYADSVKG

                    FW 3                                CDR 3                FW 4
VH3_DP51        RFTISRDNAKNSLYLQMNSL--RDEDTAVYYCAR.....................................
S1R2C_CS_1H12   RFTISRDSAKNSVSLQMNSL--RDEDTAVYYCASYYSYYY----------------GMDAWGQGTMVTV.
```

Figure 2J

```
                    FW 1                    CDR 1        FW 2                CDR 2
VH3_DP50        QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMH----WVRQAPGKGLEWVAVIWY-----DGSNKYYADSVKG
S1R3B1_BMV_1H11 EVQLVQSGGGLVKPGGSLRLSCAASGFTFSSYGMH----WVRQAPGKGLEWVAGIFY-----DGGNKYYADSVKG
S1R3B2_BMV_1E1  EVQLVETGGGVVQPGGSLSLSCAASGFTFSSYGMQ----WVRQAPGKGLEWVAFIRY-----DGSSEYYADSVKG
S1R3B1_BMV_1H5  QVQLQESGGGVVQPGGSLRLSCAASGFTFSGYGMH----WVRQAPGKGLEWVASVRN-----DGSNTYYTDSVKD
S1R3B2_BMV_1H5  EVQLVQSGGGLVRPGGSLRLSCAASGFSFSDYYMT----WIRQIPGKGLEWVAVIWN-----DGSDRYYADSVKG

                    FW 3                                CDR 3                FW 4
VH3_DP50        RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCAR.....................................
S1R3B1_BMV_1H11 RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCARDRGYYYM----------------DVWGKGTTVTVSS.
S1R3B2_BMV_1E1  RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCGRTLES------------------SLWGKGTLVTVSS.
S1R3B1_BMV_1H5  RFTISRDNTKNTLYLQMNSL--RAEDTAVYYCAKSRRVMYGTSYYF----------DYWGRGTLVTVSS.
S1R3B2_BMV_1H5  RFTISRDNSKNTLFLQMSSL--RDEDTALYYCVRGGPTASSGF-------------DYWGRGTLVTVSS.
```

Figure 2K

```
                    FW 1                    CDR 1        FW 2                    CDR 2
VH3_DP49            QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMH----WVRQAPGKGLEWVAVISY-----DGSNKYYADSVKG
S1R3B1_BMV_1C12     EVQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMH----WVRQAPGKGLEWVAVISY-----DGSIKYYADSVKG
S1R3B1_BMV_1A10     QMQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMH----WVRQAPGKGLEWVAVISY-----DGSIKYYADSVKG

                    FW 3                                    CDR 3                FW 4
VH3_DP49            RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCAK.....................................
S1R3B1_BMV_1C12     RFTISRDNSKNTLYLQMNSL--RAEDTAVYYCARTGEYSGYDTSGY----------SNWGQGTLVTVSS.
S1R3B1_BMV_1A10     RFTISRDNSKNTLYLQMNSL--RAEDTGVYYCSKDRYSSGWYSSDAF---------DIWGRGTMVTVSS.
```

Figure 2L

```
                    FW 1                    CDR 1        FW 2                    CDR 2
VH1_DP8             QVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMH----WVRQAPGQGLEWMGWINPN----SGGTNYAQKFQGW
S1R2A_CS_1F7_1      EVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMH----WVRQAPGQGLEWMGWINPN----SGGTNYAQKFQGW
S1R3A1_CS_1B12      QVQLVQSGAEVKKPGASVKVSCQASGYTFSGHYMH----LVRQAPGQGLEWMGWIHP-----TSGGTTYAQKFQG
S1R2A_CS_1D3_1      EVQLVQSGAEVKKPGASVKVSCKASGYSFTAFYIH----WVRQAPGQGLEYLGWIDP-----NTGATKYAQRFQG
S1R3A1_CS_1B10      EVQLVQSGAEVKKPGASVRVSCKGSGNTFTGHYIH----WVRQAPGQGLEWLGWIDP-----NTGDIQYSENFKG

                    FW 3                                    CDR 3                FW 4
VH1_DP8             VTMTRDTSISTAYMELSRL---RSDDTAVYYCAR.....................................
S1R2A_CS_1F7_1      VTMTRDTSISTAYMELSRL---RSDDTAVYYCARDSTMAPGAF----------DIWGRGTLVTVSS.
S1R3A1_CS_1B12      RVVMTRDTSISTAYMELSRL--TSDDTAVYYCARMSQNYDAF----------DIWGQGTMVTVSS.
S1R2A_CS_1D3_1      RVIMTWDTSITTATMELSRL--TSDDSAVYYCVRDLREWGYELSV-------EYWGRGTLVTVSS.
S1R3A1_CS_1B10      SVTLTRDPSINSVFMDLIRL--TSDDTAMYYCAREGAGLANYYYYGL----------DVWGRGTMVTVSS.
```

Figure 2M

```
                  FW 1                      CDR 1                FW 2          CDR 2
VK1_L12           DIQMTQSPSTLSASVGDRVTITCRASQ--------SISSWLAWYQQKPGKAPKLLIYKA-----SSLES
S1R3B2_BMV_1G2    DIQMTQSPSTLSASIGDRVTITCRASE--------GIYHWLAWYQQKPGKAPKLLIYKA-----SSLAS

                        FW 3                          CDR 3          FW 4
VK1_L12           GVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYN.............................
S1R3B2_BMV_1G2    GAPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYSNYP---------LTFGGGTKLEI---KRA.
```

Figure 3A

```
                  FW 1                      CDR 1                FW 2          CDR 2
VK1_L12           DIQMTQSPSTLSASVGDRVTITCRASQ--------SISSWLAWYQQKPGKAPKLLIYKA-----SSLES
S1R3C1_BMV_1H11   DIQMTQSPSTLSASIGDRVTITCRASE--------GIYHWLAWYQQKPGKAPKLLIYKA-----SSLAS

                        FW 3                          CDR 3          FW 4
VK1_L12           GVPSRFSGSGSGTEFTLTISSLQPDDFATYYCQQYN.............................
S1R3C1_BMV_1H11   GAPSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYSNYP---------LTFGGGTKLEI---KRA.
```

Figure 3B

	FW 1	CDR 1	FW 2	CDR 2
VL1_DPL2	QSVLTQPPS-ASGTPGQRVTISC	SGSSSN------	IGSNTVNWYQQLPGTAPKLLIY	SN-----NQRPS
S1R2C_CS_1H12	SYVLTQPPS-ASGTPGQRVTISC	SGSSSN------	IGSNTVNWYQQLPGTAPKLLIY	SN-----NQRPS
S1R3C1_CS_1A6	QSVLTQPPS-ASGTPGQRVTISC	SGSSSN------	IGTNTVNWYQQLPGTAPKLLIY	TS-----NQRPS
S1R3A1_DP47_1A6	HVILTQPPS-ASGTPGQRVTISC	SGSSSN------	IGSNSVSWYQQLPGTAPKLLMY	TN-----NQRPS
S1R3B1_BMV_1C12	QSVLTQPPS-ASGTPGQRVTISC	SGSSSN------	IGSNTVNWYQRLPGAAPQLLIY	NN-----DQRPS
S1R3B2_DP47_1C9	QSVLTQPPS-ASGTPGQTVTISC	SGSSSN------	IGSSVVNWYQQFPGTAPKVLVY	SN-----TQRPS

	FW 3	CDR 3	FW 4
VL1_DPL2	GVPDRFSGSKSGTSASLAISGLQSEDEADYYC	AAWD	.....
S1R2C_CS_1H12	GVPDRFSGSKSGTSASLAISGLRSEDEADYYC	AAWDYSLSG-------WV	FGGGTKVTV---LGA.
S1R3C1_CS_1A6	GVPARFSASNSGTSASLAISGLRSEDEADYYC	AAWDDKLSG-------AV	FGGGTKLTV---LGA.
S1R3A1_DP47_1A6	GVPDRFSGSKSGTSASLAISGLQSEDEADYYC	ATWDASLNT-------WV	FGGGTKVTV---LGA.
S1R3B1_BMV_1C12	GIPDRFSGSKSGTSGSLVISGLQSEDEADYYC	ASWDDSLNG-------RV	FGGGTKLTV---LGA.
S1R3B2_DP47_1C9	GVPDRFSGSRSGTSASLAISGLQSEDEADYYC	LAWDASLNG-------WV	FGGGTKLTV---LGA.

Figure 3C

	FW 1	CDR 1	FW 2	CDR 2
VL8_DPL21	QTVVTQEPS-FSVSPGGTVTLTC	GLSSGSV-----	STSYYPSWYQQTPGQAPRTLIY	ST-----NTRSS
S1R3A1_CS_1D11	QAVVLQEPS-FSVSPGGTVTLTC	GLRSGSV-----	STSHYPSWYQQTPGQAPRTLIY	ST-----NTRSS
S1R3A1_CS_1B9	QTVVIQEPS-FSVSPGGTVTLTC	GLSSGSV-----	STSYYPSWYRQTPGQAPHTLIH	NT-----KIRSS
S1R3A1_CS_1B10	QTVVLQEPS-FSVSPGGTVTLTC	GLNFGSV-----	STAYYPSWYQQTPGQAPRTLIY	GT-----NIRSS

	FW 3	CDR 3	FW 4
VL8_DPL21	GVPDRFSGSILGNKAALTITGAQADDESDYYC	VLYM	.....
S1R3A1_CS_1D11	GVPDRFSGSILGNKAALTITGAQADDESNYYC	MLYMGSGM--------YV	FGGGTKVTV---LGA.
S1R3A1_CS_1B9	GVPDRFSGSILGNNAALTITGAQADDESDYYC	LLYMGSGI--------YV	FGGGTKLTV---LGA.
S1R3A1_CS_1B10	GVPDRFSGSIVGNKAALTITGAQTEDESDYYC	ALYMGSG---------ML	FGGGTKVTV---LGA.

Figure 3D

```
                    FW 1                    CDR 1                FW 2          CDR 2
VL6_6a              NFMLTQPHS-VSESPGKTVTISCTRSSGS------IASNYVQWYQQRPGSSPTTVIYED-----NQRPS
S1R3C1_CS_1B10      NFMLTQPHS-VSESPGKTVTISCTGSSGS------IASNYVQWYQQRPDSAPTTVIYED-----NRRSS
S1R3B1_DP47_1E1     NFMLTQPHS-VSGSPGKTVTISCTRSSGY------IDSKYVQWYQQRPGSAPTTVIYED-----NRRPS

                    FW 3                              CDR 3          FW 4
VL6_6a              GVPDRFSGSIDSNSASLTISGLKTEDEADYYCQSYD.............................
S1R3C1_CS_1B10      GVPDRFSGSIDSNSASLSISGLKTEDEADYYCQSYDSSGH--------VVFGGGTKLTV---LGA.
S1R3B1_DP47_1E1     GVPDRFSGSIDSNSASLTISGLETEDEADYYCQSYDDTN---------VVFGGGTKVTV---LGA.
```

Figure 3E

```
                    FW 1                    CDR 1                FW 2          CDR 2
VL3_DPL16           SSELTQDPA-VSVALGQTVRITCQGDS--------LRSYYASWYQQKPGQAPVLVIYGK-----NNRPS
S1R3B1_BMV_1H5      SSELTQDPA-VSVALGQTVRITCQGDS--------LRSYYASWYQQKPGQAPVLVIYGK-----NNRPS
S1R3B1_BMV_1H9      SSELTQDPA-VSVALGQTVRITCQGDS--------LRSYYASWYQQKPGQAPVLVIYGK-----NNRPS
S1R3A1_BMV_1F3      SSELTQDPA-VSVALGQTVRITCQGDS--------LRSYYASWYQQKPGQAPVLVIYGK-----NNRPS
S1R3B1_BMV_1A10     SSELTQDPA-VSVALGQTVRITCQGDS--------LRSYYASWYQQKPGQAPVLVIYGK-----NNRPS

                    FW 3                              CDR 3          FW 4
VL3_DPL16           GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRD.............................
S1R3B1_BMV_1H5      GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNH-------VVFGGGTKLTV---LGA.
S1R3B1_BMV_1H9      GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNH-------VVFGGGTKLTV---LGA.
S1R3A1_BMV_1F3      GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNH-------VVFGGGTKLTV---LGA.
S1R3B1_BMV_1A10     GIPDRFSGSSSGNTASLTITGAQAEDEADYYCHSRDSSGNH-------VLFGGGTKLTV---LGA.
```

Figure 3F

```
                    FW 1                    CDR 1                FW 2          CDR 2
VL3_3h              SYVLTQPPS-VSVAPGQTARITCGGNN--------IGSKSVHWYQQKPGQAPVLVVYDD-----SDRPS
S1R2A_CS_1F7_1      QSVLTQPPS-VSVAPGQTARMTCGGNN--------IESKTVHWYQQKPGQAPVLVVYND-----NVRPS
S1R3C1_DP47_1H1     QSVLTQPPS-VSVAPGQTARITCGGDK--------IGHKSVHWYQQKPGQAPVLLVYDD-----RKRPS

                              FW 3                         CDR 3          FW 4
VL3_3h              GIPERFSGSNSGNTATLTISRVEAGDEADYYCQVWD.............................
S1R2A_CS_1F7_1      GIPARFSGSNSGNTATLTINRVEAGDEADYYCQVWDSSRDQ-------GVFGGGTKLTV---LGA.
S1R3C1_DP47_1H1     GIPERFSGSNSGNTATLTISRVEAGDEAAYHCQVWDRSSDP-------YVFGTGTKVTV---LGA.
```

Figure 3G

```
                    FW 1                    CDR 1                FW 2          CDR 2
VL2_DPL11           QSALTQPAS-VSGSPGQSITISCTGTSSDV-----GGYNYVSWYQQHPGKAPKLMIYEV-----SNRPS
S1R3B1_BMV_1G11     QSVLTQPAS-VSGSPGQSITISCTGTSSDV-----GGYNYVSWYQQHPGKAPKLMIYEG-----SKRPS
S1R3A1_BMV_1G4      QSVLTQPAS-VSGSPGQSITISCTGTSSDV-----GGYNYVSWYQQHPGKAPKLMIYEG-----SKRPS
S1R3B1_BMV_1A1      QSVLTQPAS-VSGSPGQSITISCTGTSSDV-----GGYNYVSWYQQHPGKAPKLMIYEG-----SKRPS
S1R3B2_BMV_1H5      SSELTQPAS-VSGSPGQSITISCTGTSSDV-----GGYNYVSWYLQHPGKAPKLMIYEG-----SKRPS

                              FW 3                         CDR 3          FW 4
VL2_DPL11           GVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYT.............................
S1R3B1_BMV_1G11     GVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRST--------RVFGGGTKLTV---LGA.
S1R3A1_BMV_1G4      GVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRST--------RVFGGGTKLTV---LGA.
S1R3B1_BMV_1A1      GVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRST--------RVFGGGTKLTV---LGA.
S1R3B2_BMV_1H5      GVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRST--------RVFGGGTKLTV---LGA.
```

Figure 3H

```
                    FW 1                    CDR 1                FW 2          CDR 2
VL2_2c              QSALTQPPS-ASGSPGQSVTISCTGTSSDV-----GGYNYVSWYQQHPGKAPKLMIYEV-----SKRPS
S1R3C1_CS_1D3       QSVLTQPPS-ASGSPGQSVTISCTGTSSDV-----GAYDFVSWYQQHPGKAPKLMIYEV-----NKRPS

                          FW 3                          CDR 3          FW 4
VL2_2c              GVPDRFSGSKSGNTASLTVSGLQAEDEADYYCSSYA.............................
S1R3C1_CS_1D3       GVPDRFSGSKSGNTASLTVSGLQAEDEADYYCSSYAGSKN--------LLFGGGTKLTV---LGA.
```

Figure 3I

```
                    FW 1                    CDR 1                FW 2          CDR 2
VL1_DPL8            QSVLTQPPS-VSGAPGQRVTISCTGSSSNI-----GAGYDVHWYQQLPGTAPKLLIYGN-----SNRPS
S1R3B1_BMV_1H11     QSVLTQPPS-VSGAPGQRVTISCTGRSSNI-----GAGHDVHWYQQLPGTAPKLLIYGD-----SNRPS
S1R3A1_CS_1B12      QAVLTQPSS-VSGAPGQRVTISCTGSSSNI-----GAGYDVNWYQQFPGTAPKIIVY-------GDRPS
S1R3B2_DP47_1E8     QAVLTQPSA-VSGAPGQRVTISCTGTSSNI-----GTNYLVHWYQQRPGTAPQLLVSGN-----NTRPS

                          FW 3                          CDR 3          FW 4
VL1_DPL8            GVPDRFSGSKSGTSASLAITGLQAEDEADYYCQSYD.............................
S1R3B1_BMV_1H11     GVPDRFSGSRSGTSASLAITGLQAEDEADYYCQSYDSSLRG-------SVFGGGTKVTV---LGA.
S1R3A1_CS_1B12      GAPDRFSGSKSGTSASLAITGLRAEDEADYYCQSWDSRLSS-------YVFGTGTKVTV---LGA.
S1R3B2_DP47_1E8     GVTDRFSVSKSATSASLAITGLQAEDEADYYCQTYDINLRV-------WVFGGGTKVTV---LGA.
```

Figure 3J

```
                    FW 1                    CDR 1                FW 2          CDR 2
VL1_DPL5            QSVLTQPPS-VSAAPGQKVTISCSGSSSN------IGNNYVSWYQQLPGTAPKLLIYDN-----NKRPS
S1R2C_CS_1D3        QSVLTQPPS-VSAAPGQKVTISCSGGRSS------IGNNYVSWYQHLPGTAPKLLIYDN-----NQRPS
S1R2A_CS_1D11       QAVLTQPSS-VSAAPGQEVSISCSGARSN------VGGNYVSWYQHLPGTAPKLLIYDN-----NKRPS
S1R3B2_BMV_1E1      QSVLTQPPS-VSAAPGQKVTISCSGSTSN------IGNNYVSWYQQHPGKAPKLMIYDV-----SKRPS

                    FW 3                    CDR 3          FW 4
VL1_DPL5            GIPDRFSGSKSGTSATLGITGLQTGDEADYYCGTWD.............................
S1R2C_CS_1D3        GIPDRFSGSKSGTSATLGITGLQTGDEADYYCGTWDSSLSA-------VVFGGGTKVTV---LGA.
S1R2A_CS_1D11       GMPDRFSGSKSGTSATLGITGVQTEDEADYYCATWDSSLSA-------VVFGGGTKLTV---LGA.
S1R3B2_BMV_1E1      GVPDRFSGSKSGNSASLDISGLQSEDEADYYCAAWDDSLSE-------FLFGTRTKLTV---LGA.
```

Figure 3K

```
                    FW 1                    CDR 1                FW 2          CDR 2
VL1_DPL3            QSVLTQPPS-ASGTPGQRVTISCSGSSSN------IGSNYVYWYQQLPGTAPKLLIYRN-----NQRPS
S1R2A_CS_1D3_1      QSVLTQPPS-ASGTPGQRVTISCSGSSSN------IGSNYVYWYQQLPGTAPKLLIYRN-----NQRPS
S1R3B2_DP47_1E10    HVILTQPPS-TSGTPGQTVTISCSGSSSN------IGSHYVYWYQQLPGTAPKLLIYRN-----NQRPS

                    FW 3                    CDR 3          FW 4
VL1_DPL3            GVPDRFSGSKSGTSASLAISGLRSEDEADYYCAAWD.............................
S1R2A_CS_1D3_1      GVPDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLSG-------WVFGGGTKLTV---LGA.
S1R3B2_DP47_1E10    GVPDRFSGSKSGTSASLAISGLRSEDETDYYCAAWDDSLSG-------RVFGTGTKLTV---LGA.
```

Figure 3L

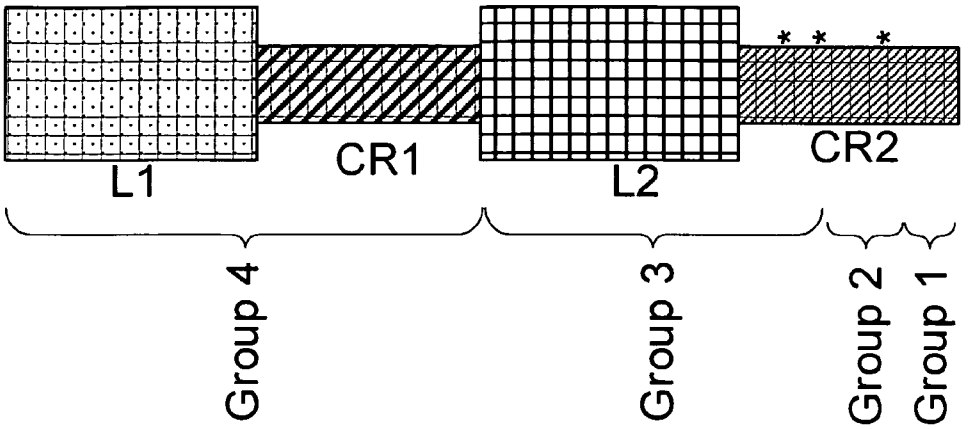


Figure 4B

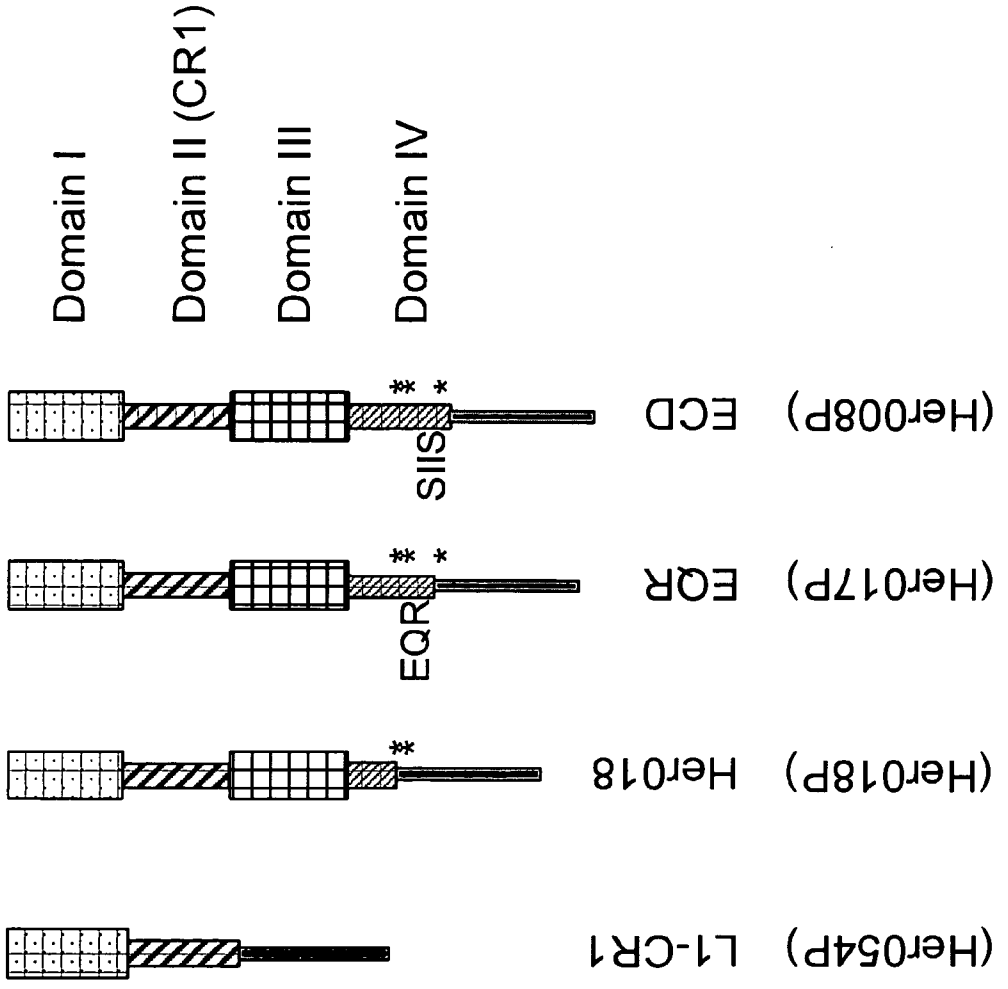


Figure 4A

		ScFv ON PHAGE BINDING TO CELLS			ScFv BINDING TO PURIFIED PROTEINS IN ELISA			
SMIP NAME	ScFv CLONE NAME	CHO-ECD	CHO-CR2	SKBR3	ECD	EQR	Her018	L1-CR1
HER026	S1R2A_CS_1D11	++	++	++	-	-	-	-
HER027	S1R2C_CS_1D3	++	++	++	+/-	+/-	-	-
HER028	S1R2A_CS_1D3_1	++	++	+	-	-	-	-
HER029	S1R2A_CS_1F7_1	++	++	++	-*	-*	-*	-
HER030	S1R3B2_BMV_1H5	++	++	+	-*	-*	-*	-
HER031	S1R3C1_CS_1D3	++	++	++	+	+	-	-
HER032	S1R3B2_DP47_1E10	++	++	++	-	-	-	-
HER033	S1R3C1_CS_1B10	++	++	++	++	+	++	-
HER034	S1R3C1_CS_1A6	++	++	+	-*	-*	-*	-
HER035	S1R3B2_DP47_1E8	++	++	+	-*	-*	-	-
HER036	S1R3B2_BMV_1E1	++	++	++	-	-	-	-
HER037	S1R3B2_BMV_1G2	++	++	+	+	+	+	-
HER038	S1R3B2_DP47_1C9	++	++	+	-*	-*	-	-
HER039	S1R2C_CS_1H12	++	++	++	-	-	-	-
					ECD	EQR	Her018	L1-CR1
HER071	S1R3A1_BMV_1F3				+++	+++	+++	-
HER072	S1R3A1_BMV_1G4				-	-	-	-
HER073	S1R3A1_CS_1B9				+	+	+	+
HER074	S1R3A1_CS_1B10				+/-	+	+	+
HER075	S1R3A1_CS_1B12				+/-	+	-	-
HER076	S1R3A1_CS_1D11				-	-	-	-
HER077	S1R3A1_DP47_1A6				+	+	+	-
HER078	S1R3B1_BMV_1A1				++	+	-	-
HER079	S1R3B1_BMV_1A10				-	-	-	-
HER080	S1R3B1_BMV_1C12				+/-	-	-	-
HER081	S1R3B1_BMV_1G11				+/-	-	-	-
HER082	S1R3B1_BMV_1H5				+/-	-	-	-
HER083	S1R3B1_BMV_1H9				+/-	-	-	-
HER084	S1R3B1_BMV_1H11				++	++	++	++
HER085	S1R3B1_DP47_1E1				+	-	-	-
HER086	S1R3C1_BMV_1H11				-	-	-	-
HER087	S1R3C1_DP47_1H1				-	-	-	-

Figure 5

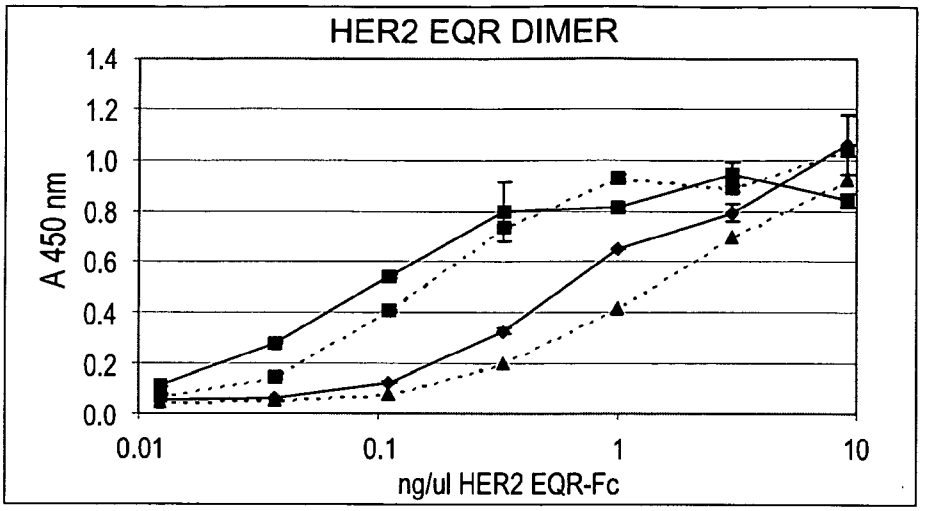


Figure 6A

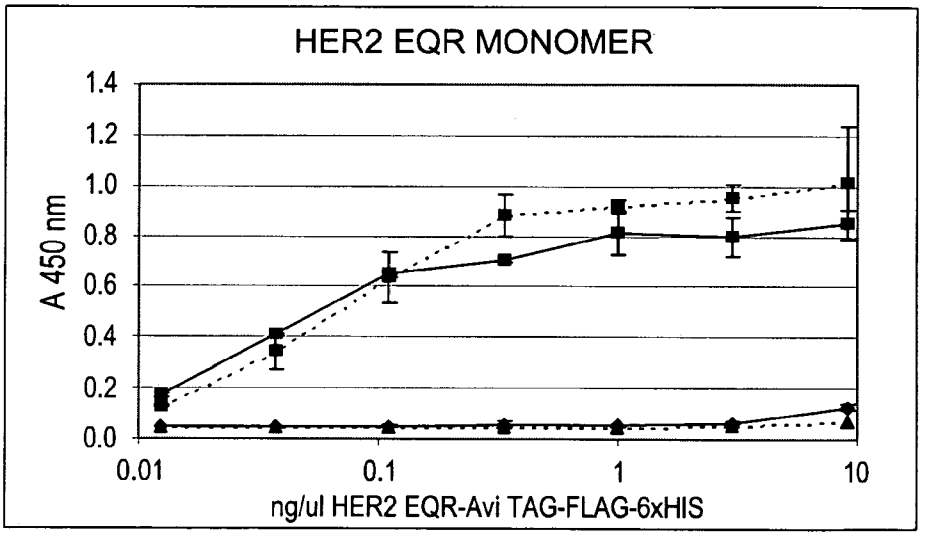


Figure 6B

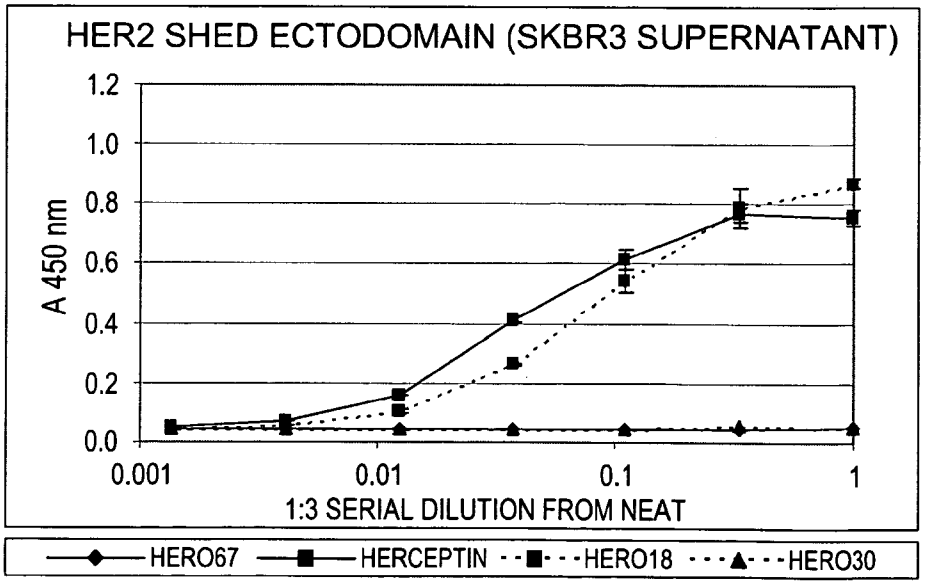


Figure 6C

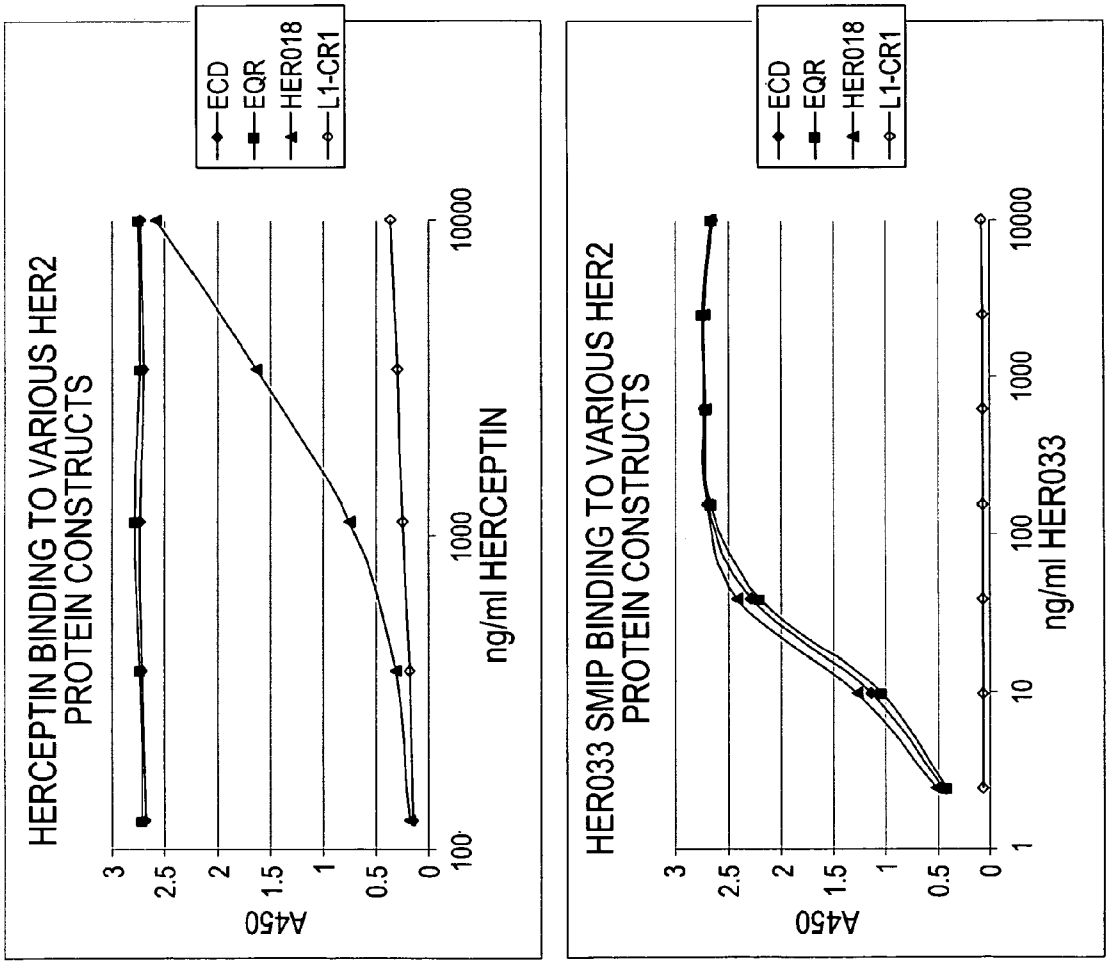
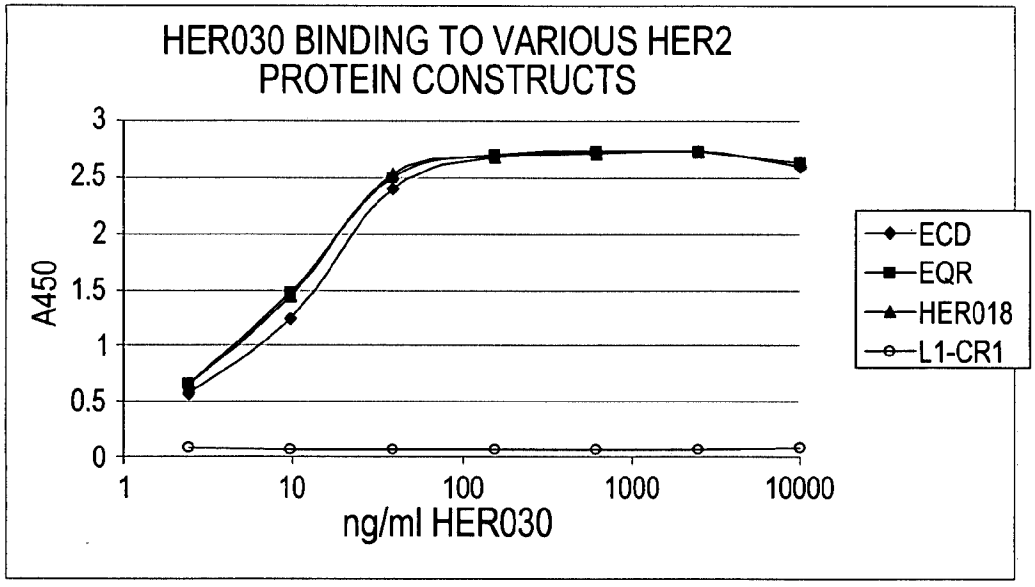

HERCEPTIN BINDING TO VARIOUS HER2 PROTEIN CONSTRUCTS
ECD
EQR
HER018
L1-CR1
A450
3
2.5
2
1.5
1
0.5
0
100
1000
10000
ng/ml HERCEPTIN
HER033 SMIP BINDING TO VARIOUS HER2 PROTEIN CONSTRUCTS
ECD
EQR
HER018
L1-CR1
A450
3
2.5
2
1.5
1
0.5
0
1
10
100
1000
10000
ng/ml HER033

Figure 7



BIACORE DATA FOR HERCEPTIN/HER018 (HERCEPTIN SMIP)/HER067 (AKA HER033) BINDING TO ECD/HER018/HER020

	K_D (M)		
	ECD	HER018	HER020
HERCEPTIN	1.06E-09	2.28E-07	NB*
HERCEPTIN SMIP (HER018)	1.40E-09	1.67E-07	NB*
HER067 (AKA HER033)	8.18E-09	6.47E-09	NB*
HER030	3.56E-08	2.76E-08	NB*

*NB; NO BINDING

Figure 7 (continued)

Trubion	ELISA							Cell Binding									
name	SIIS	EQR	1.8	1.6	1	muSIIS	mcSIIS	CHOCR2	SKBR3	BT474	MDA-MB-453	MDA-MB-361 (ATCC)	MDA-MB-361 (JL)	MDA-MB-175	22rv1	CHO-muHer2	Jurkat-mcSIIS
HER026	+	+	-			-	+	++/+	++/+								
HER027	+	+	-			-	+	++/+	++/+								
HER028	+	+	++			-	+	+	+								
HER029	++	+	+++			+	+	-	++/+							+	
HER030	++	++	+++			-	+	++ *	++/+ *	+++	++	++	++	+/-	-	-	-
HER031	+	+	+			-	+	++	+++								
HER032	+	+	-			-	-	ND	ND								
HER033	++	++	+++			-	+	+++	+++/++	+++	++	+++	++	++	+/-	-	+
HER034	+	+	+			-	-	+	++/+								
HER035	+	ND	ND			ND	+	ND	ND								
HER036	+	+	+			-	+	+	+								
HER037	+	+	++			-	+	+	++/+								
HER038	++					-	+	++	++								
HER039	++	++	++			-	+	+	+								
Herceptin	+++	+++	++			-	+	+++	+++	+++	+++	+++	+++	+++	++	-	+
HER018	+					-	+			+++	+++	+++	+++	+++	++	-	+
HER071	+	+	+	+	-	+	+			++	+++					+	+
HER072	+	+	+	+	-	-	-			++	++						
HER073	+	+	+	+	+	-	+			+++	+++						
HER074	+	+	+	+	+	-	+			+	+						
HER075						-	+										
HER076	+	+	+	+	+	-	+			++	+/-						
HER077	+	+	+	-	-	-	+			++	++						
HER078	+	+	-	-	-	+	+			-	-					-	
HER079						+	+									-	
HER080	-	-	-	-	-	-	-										
HER081	-	-	-	-	-	-	-										
HER082	-	-	-	-	-	-	-										
HER083	-	-	-	-	-	-	-										
HER084	-	-	-	-	-	-	-										
HER085	+	-	-	-	-	-	+			-	-	-	-	-	-		
HER086	-	-	-	-	-	-	-			-	-						
HER087	-	-	-	-	-	-	-			-	-						

Figure 8

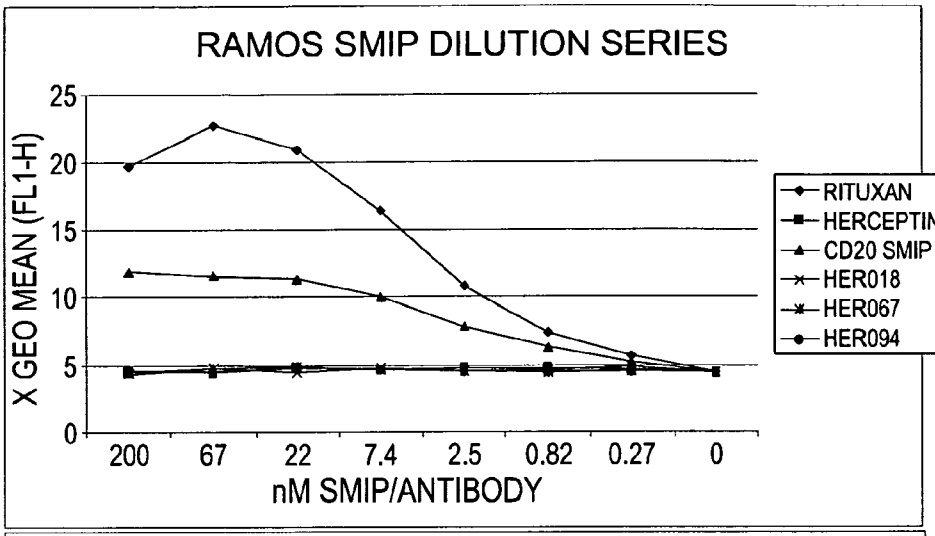


Figure 9A

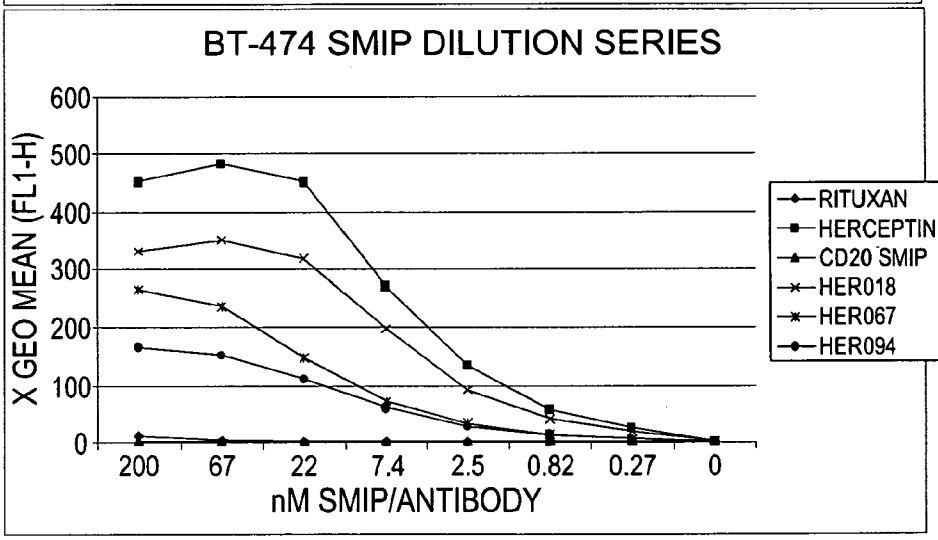


Figure 9B

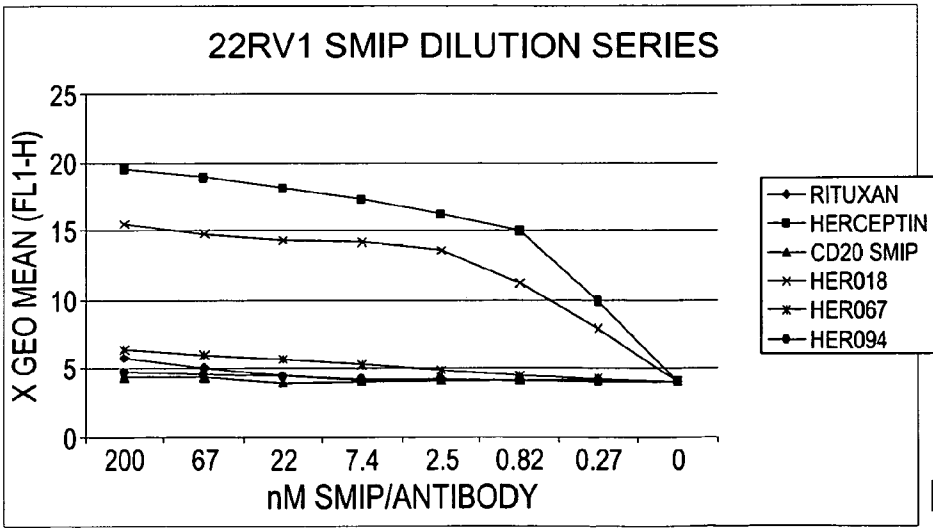


Figure 9C

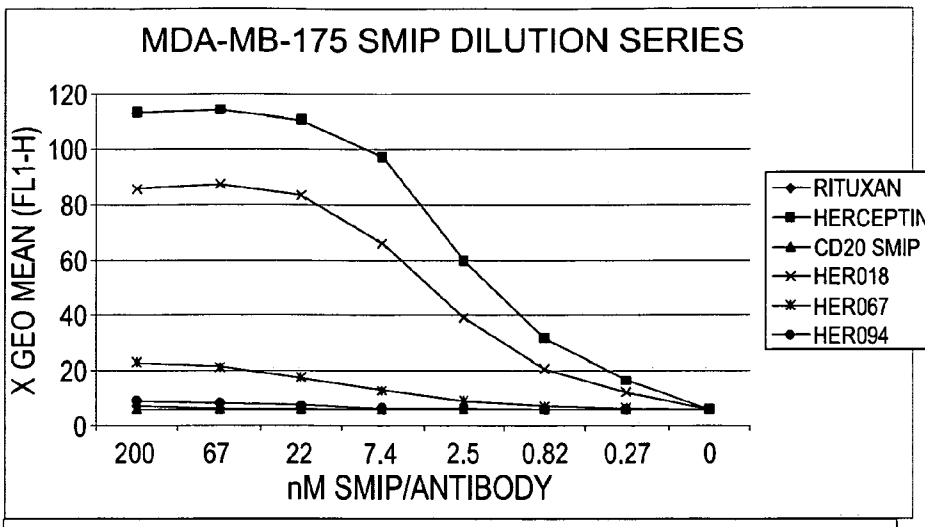


Figure 9D

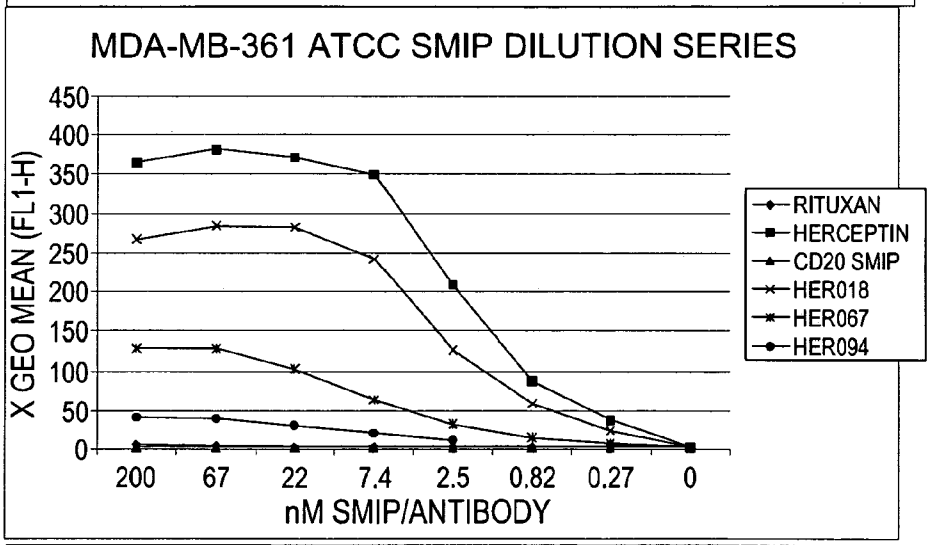


Figure 9E

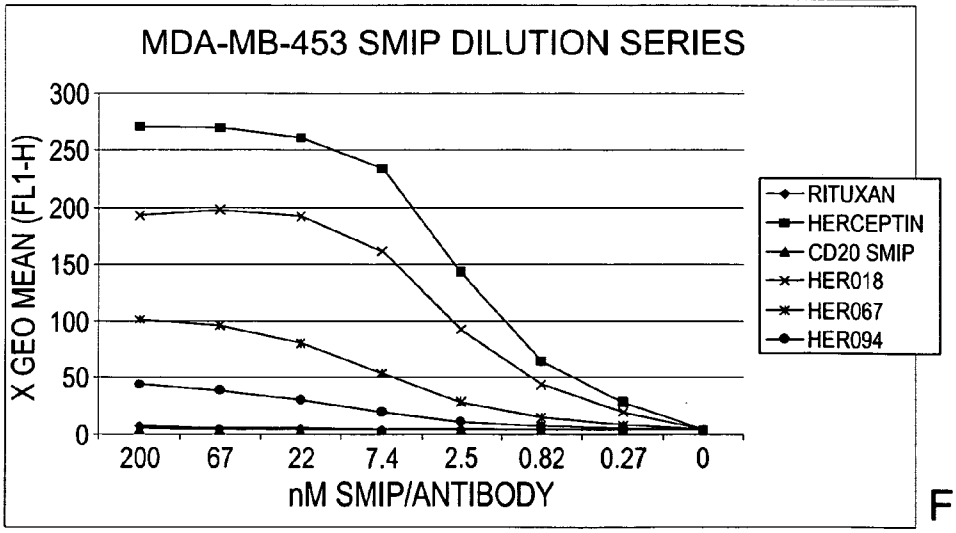


Figure 9F

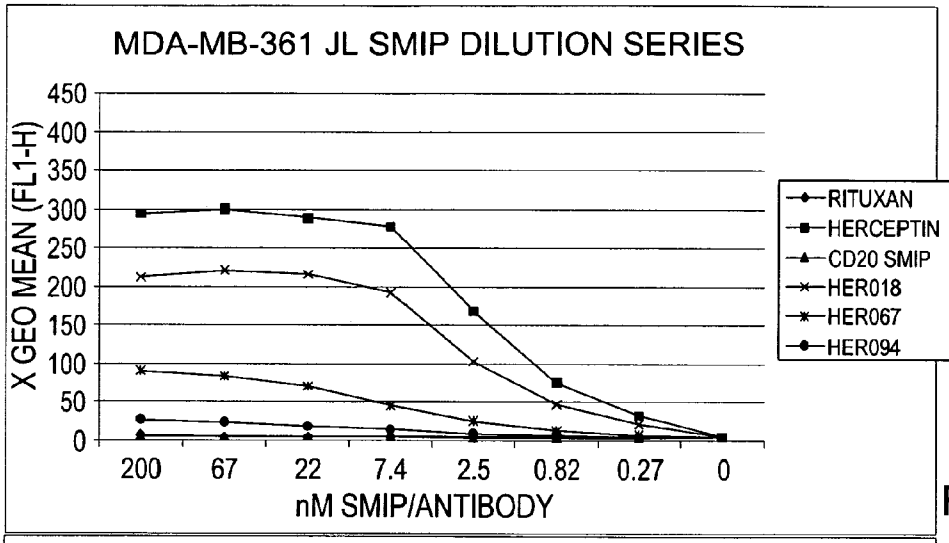


Figure 9G

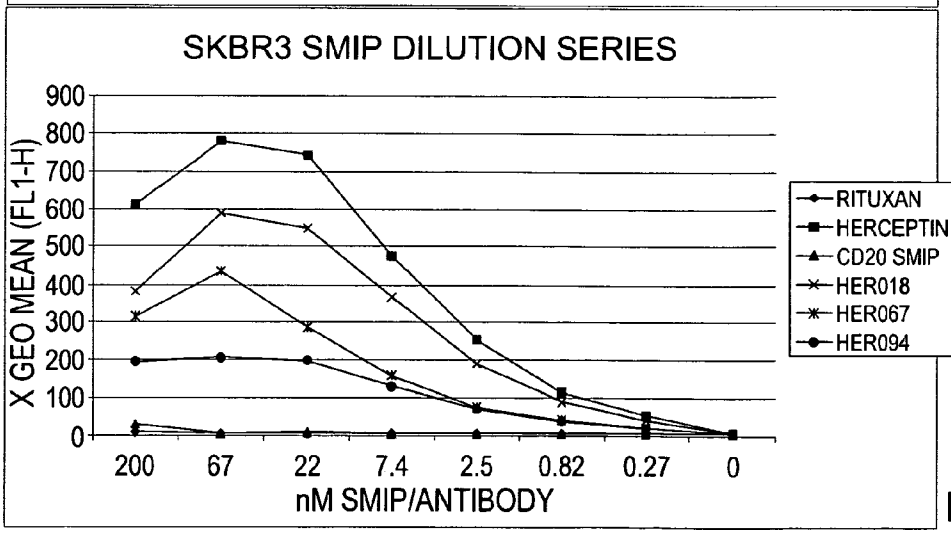


Figure 9H

CELL LINE	TYPE	ANTI-PROLIFERATION ACTIVITY	
		HERCEPTIN	HER033
SKBR3	BREAST	+	+
BT474	BREAST	+	+
MDA-MB-453	BREAST	0	+
MDA-MB-361	BREAST	0	+
JIMT	BREAST	0	0
MCF-7	BREAST	0	0
NCI-N87	GASTRIC	+	0
OVCAR-3	OVARIAN	0	0
SKOV3	OVARIAN	0	TBD

Figure 10

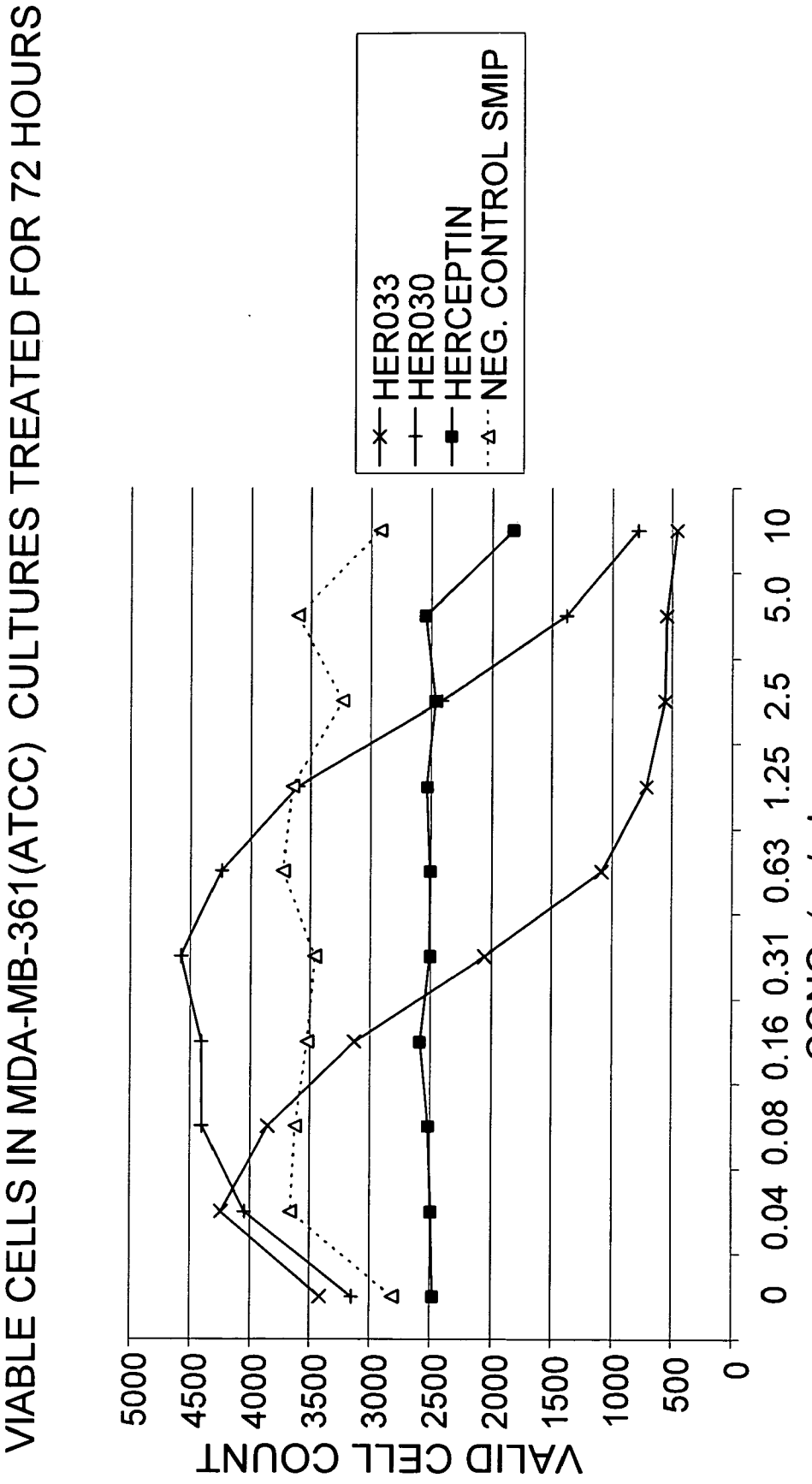

VIABLE CELLS IN MDA-MB-361(ATCC) CULTURES TREATED FOR 72 HOURS
HER033
HER030
HERCEPTIN
NEG. CONTROL SMIP
VALID CELL COUNT
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
0 0.04 0.08 0.16 0.31 0.63 1.25 2.5 5.0 10
CONC. (ug/ml)

Figure 11

Trubion	Negative Proliferation (ATP and/or BrdU)											
name	SKBR3	BT-474	MDA-MB-453	MDA-MB-361 (ATCC)	MDA-MB-361 (Wyeth)	MDA-MB-361 (JL)	JIMT	MCF-7	MDA-MB-175	NCI-N87	OVCAR-3	SKOV3
HER026	0	0										
HER027	0	0										
HER028	0	0										
HER029	0	0										
HER030	+	+	+	++					0			
HER031	0	0	0						0	0		
HER032	0	0	0						0	0		
HER033	+	+	+	++	+	+	0	0	0	0	0	0
HER034	0	0										
HER035	0	0										
HER036	0	0										
HER037	0	0	0						0	0		
HER038	0	0	0						0	0		
HER039	0	0	0									
Herceptin	+	+	0	0	0	0	0	0	+	+	0	0
HER018	+	+/-	+	+		0			+			
HER071	0		0									
HER072	0		0									
HER073	0		0									
HER074	0		0									
HER075	0		0									
HER076	0		0									
HER077	0		0									
HER078	0		0									
HER079	0		0									
HER080	0		0									
HER081	0		0									
HER082	0		0									
HER083	0		0									
HER084	0		0									
HER085	0		0									
HER086	0		0									
HER087	0		0									

Figure 12

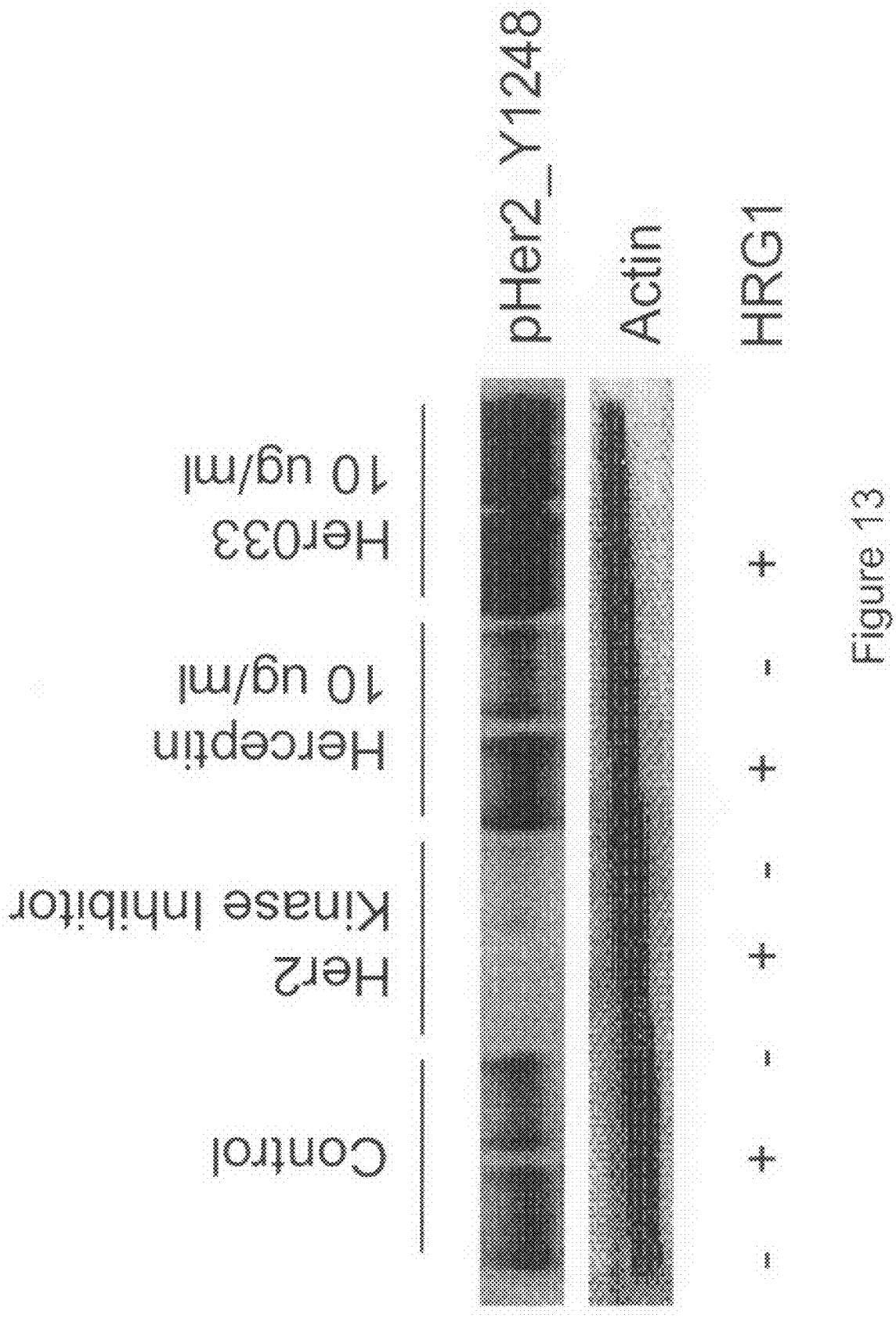

pHer2_Y1248
Actin
HRG1
- + - + - +
+ + + + + +
Control
Her2 Kinase Inhibitor
Herceptin 10 ug/ml
Her033 10 ug/ml

Figure 13

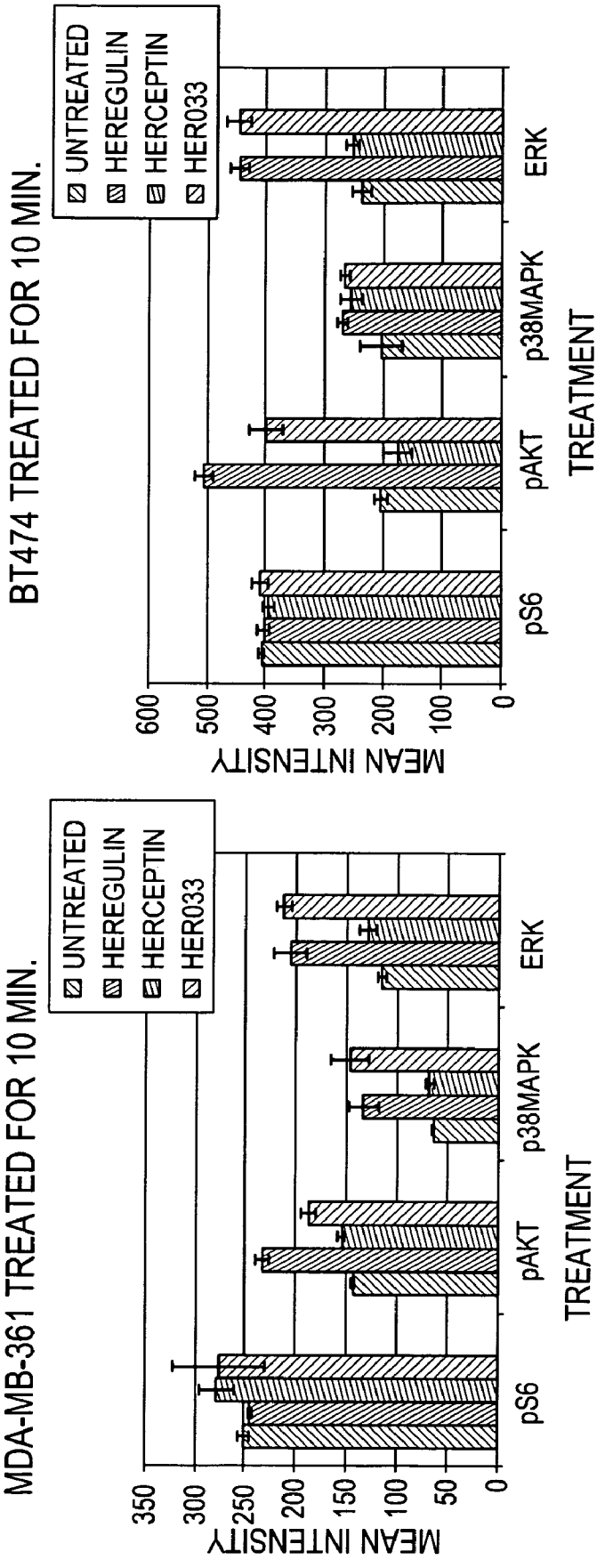

BT474 TREATED FOR 10 MIN.
UNTREATED
HEREGULIN
HERCEPTIN
HER033
MEAN INTENSITY
600
500
400
300
200
100
0
pS6
pAKT
p38MAPK
ERK
TREATMENT
MDA-MB-361 TREATED FOR 10 MIN.
UNTREATED
HEREGULIN
HERCEPTIN
HER033
MEAN INTENSITY
350
300
250
200
150
100
50
0
pS6
pAKT
p38MAPK
ERK
TREATMENT

Figure 14

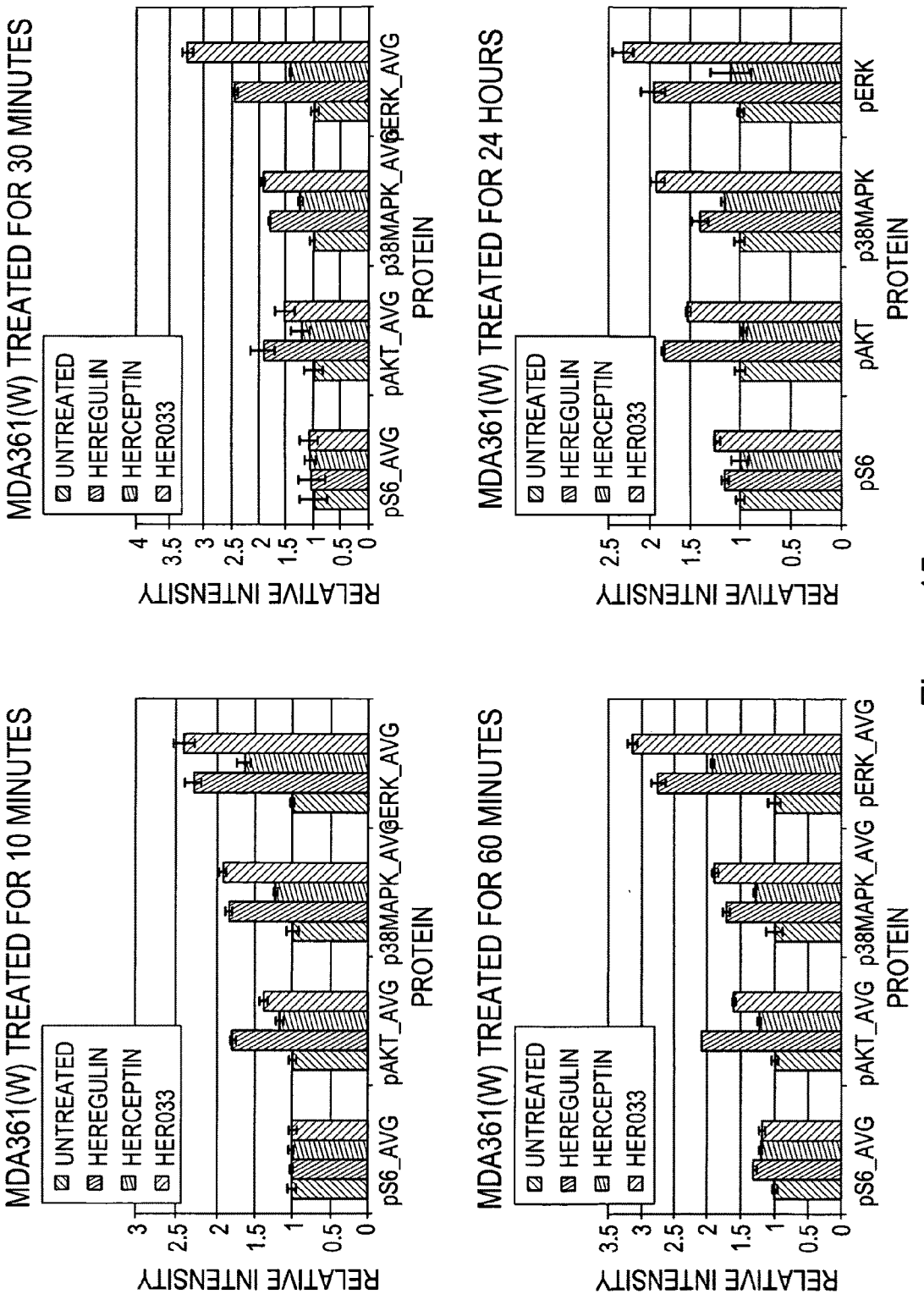

MDA361(W) TREATED FOR 30 MINUTES
UNTREATED
HEREGULIN
HERCEPTIN
HER033
RELATIVE INTENSITY
pS6_AVG
pAKT_AVG
p38MAPK_AVG
pERK_AVG
PROTEIN
MDA361(W) TREATED FOR 24 HOURS
pS6
pAKT
p38MAPK
pERK
MDA361(W) TREATED FOR 10 MINUTES
MDA361(W) TREATED FOR 60 MINUTES

Figure 15

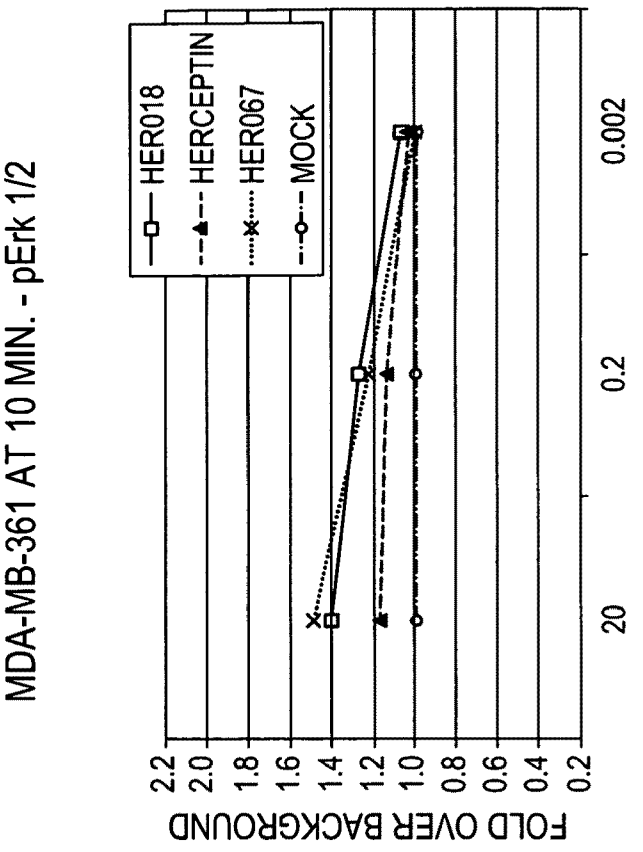


Figure 16B

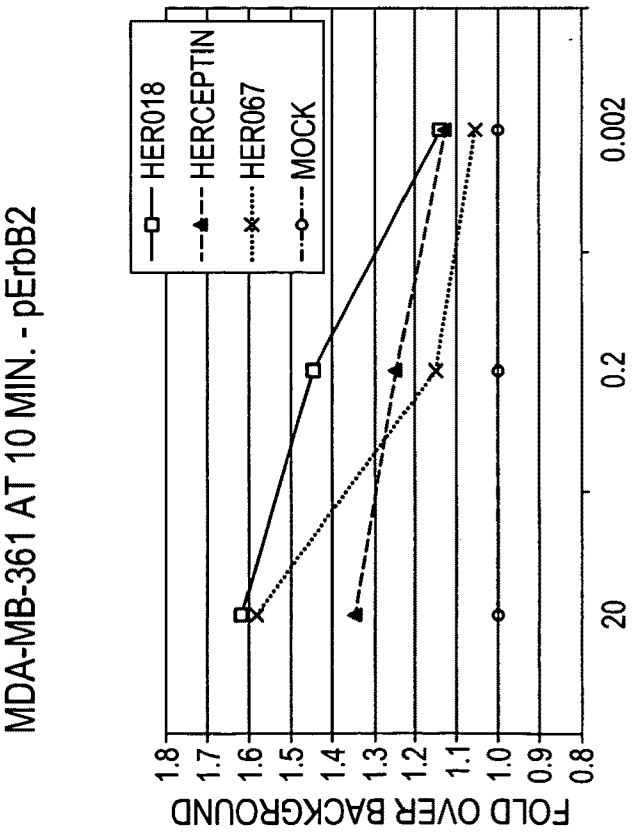


Figure 16A

HER033 and Herceptin have different effects on the cell cycle in cell lines where they are anti-proliferative.

HER033 and Herceptin have anti-proliferative effects on SKBR3 and BT474 cells.

SKBR3

	G1 phase	S phase	G2M phase
Herceptin	60.38+/- 0.65	15.53+/-0.34	16.70+/-0.32
Heregulin	32.09+/-1.33	47.54+/-0.62	11.13+/-1.46
HER033	35.65+/-1.86	48.02+/-2.31	10.78+/-1.02
control	53.98+/-2.34	24.71+/-0.86	14.54+/-1.49

BT474

	G1 phase	S phase	G2M phase
Herceptin	72.34+/-0.32	14.50+/-0.72	10.34+/-0.48
Heregulin	35.41+/-1.49	52.67+/-1.48	7.90+/-0.08
HER033	46.54+/-0.59	43.75+/-0.81	7.52+/-0.25
control	60.80+/-1.80	25.31+/-0.63	11.48+/-2.03

Values that are significantly greater are shown in light gray
Values that are significantly lower are shown in darker gray

Figure 17

HER033 has different effects on the cell cycle in Herceptin-resistant cell lines

HER033 has anti-proliferative effects on MDA-MB-453 and MDA-MB-361 cells; Herceptin has no anti-proliferative effect.

MDA-MB-453

	G1 phase	S phase	G2M phase
Herceptin	55.71+/-1.62	24.56+/-0.82	14.25+/-0.82
Heregulin	46.13+/-0.70	41.32+/-0.43	10.71+/-0.45
HER033	68.93+/-1.70	20.39+/-1.29	8.48+/-0.41
control	46.38+/-0.92	35.48+/-0.22	14.87+/-0.93

MDA-MB-361

	G1 phase	S phase	G2M phase
Herceptin	68.62+/-0.74	16.99+/-0.72	9.56+/-1.58
Heregulin	61.93+/-0.49	27.76+/-0.25	6.31+/-0.67
HER033	78.12+/-0.80	13.19+/-0.87	5.24+/-0.65
control	69.86+/-1.23	14.44+/-0.20	9.51+/-1.09

Values that are significantly greater are shown in light gray
Values that are significantly lower are shown in darker gray

Figure 18

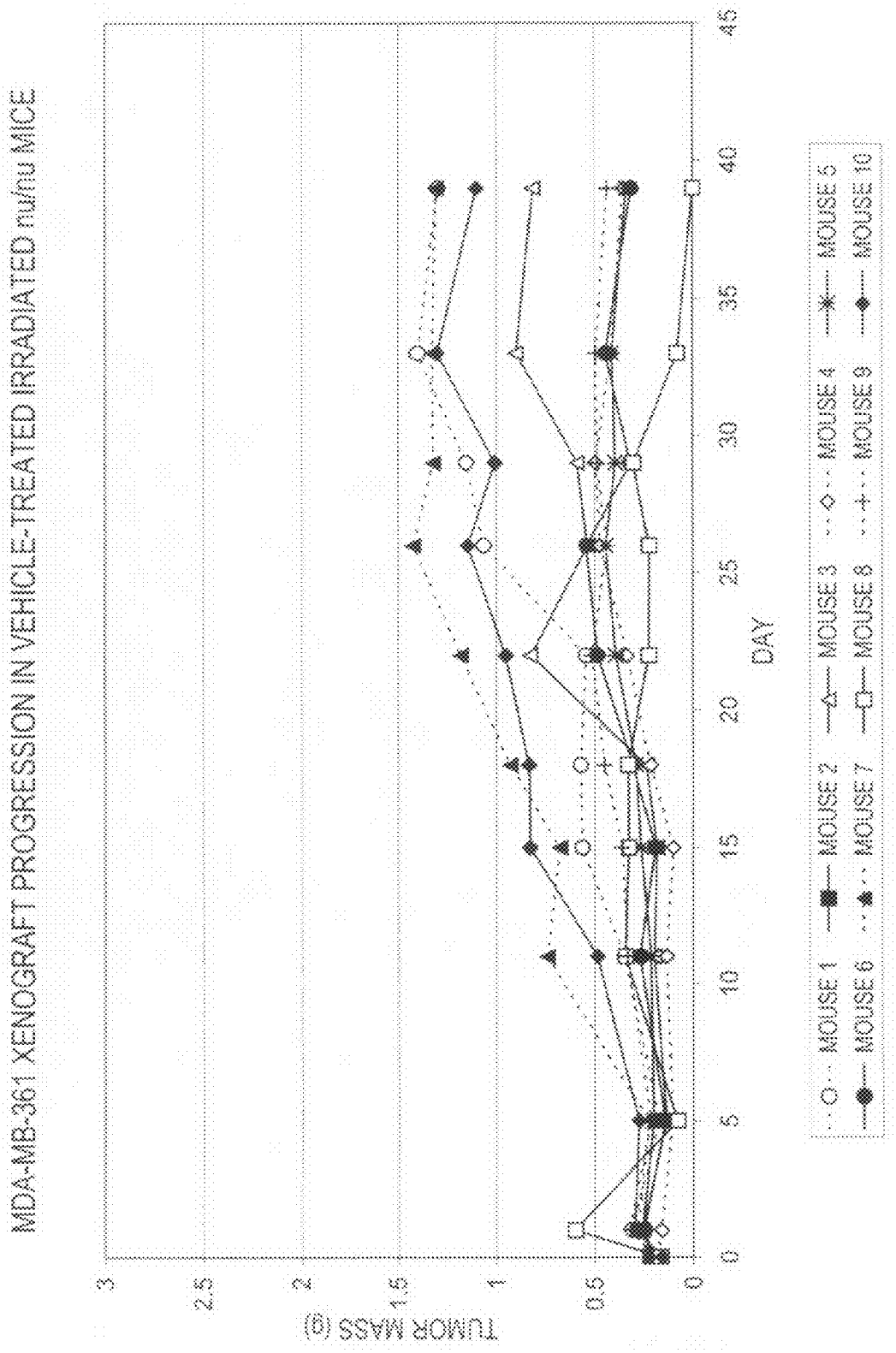

MDA-MB-361 XENOGRAFT PROGRESSION IN VEHICLE-TREATED IRRADIATED nu/nu MICE
TUMOR MASS (g)
DAY
0
0.5
1
1.5
2
2.5
3
0
5
10
15
20
25
30
35
40
45
MOUSE 1
MOUSE 2
MOUSE 3
MOUSE 4
MOUSE 5
MOUSE 6
MOUSE 7
MOUSE 8
MOUSE 9
MOUSE 10

Figure 19A

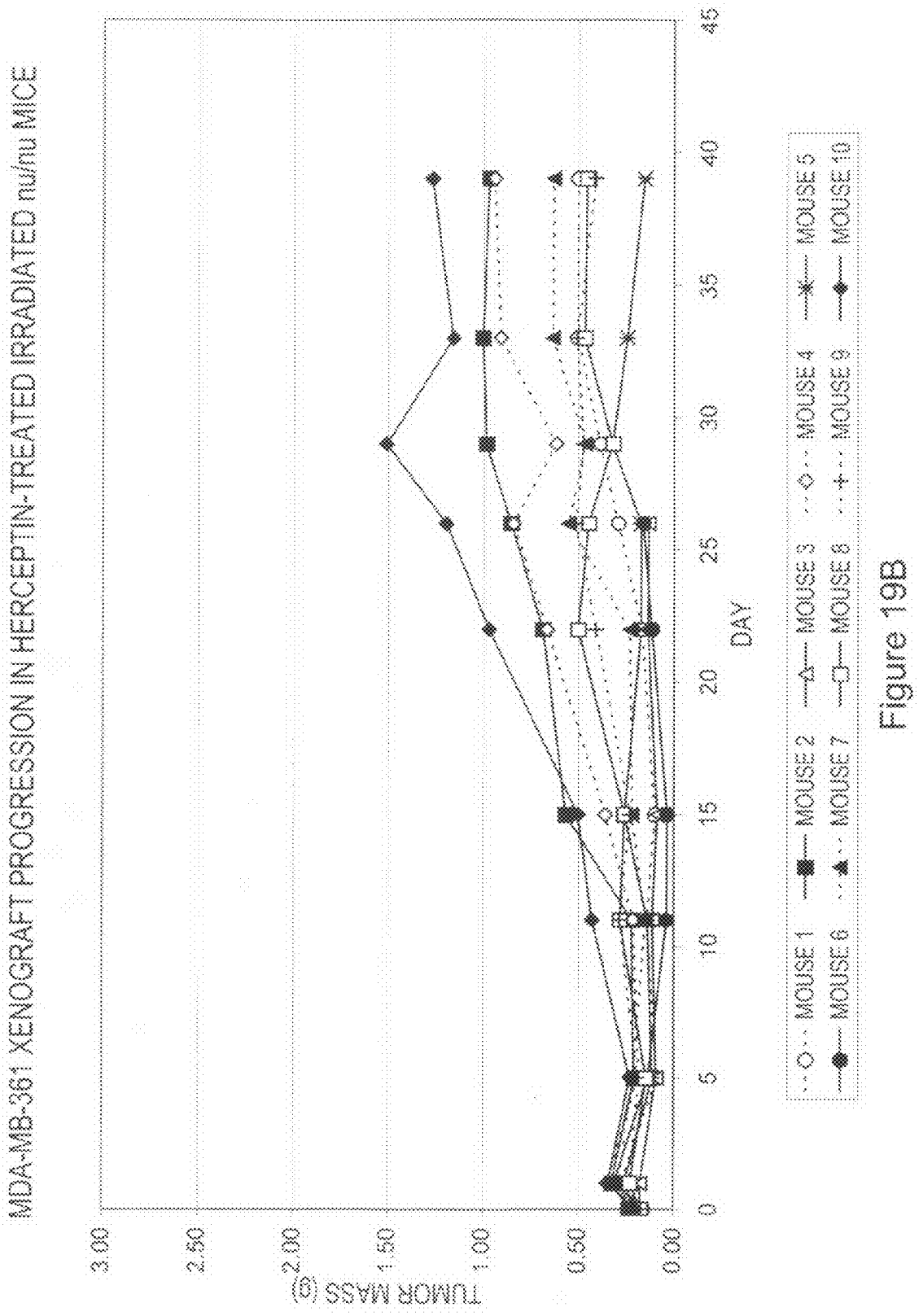

MDA-MB-361 XENOGRAFT PROGRESSION IN HERCEPTIN-TREATED IRRADIATED nu/nu MICE
TUMOR MASS (g)
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0
5
10
15
20
25
30
35
40
45
DAY
MOUSE 1
MOUSE 2
MOUSE 3
MOUSE 4
MOUSE 5
MOUSE 6
MOUSE 7
MOUSE 8
MOUSE 9
MOUSE 10

Figure 19B

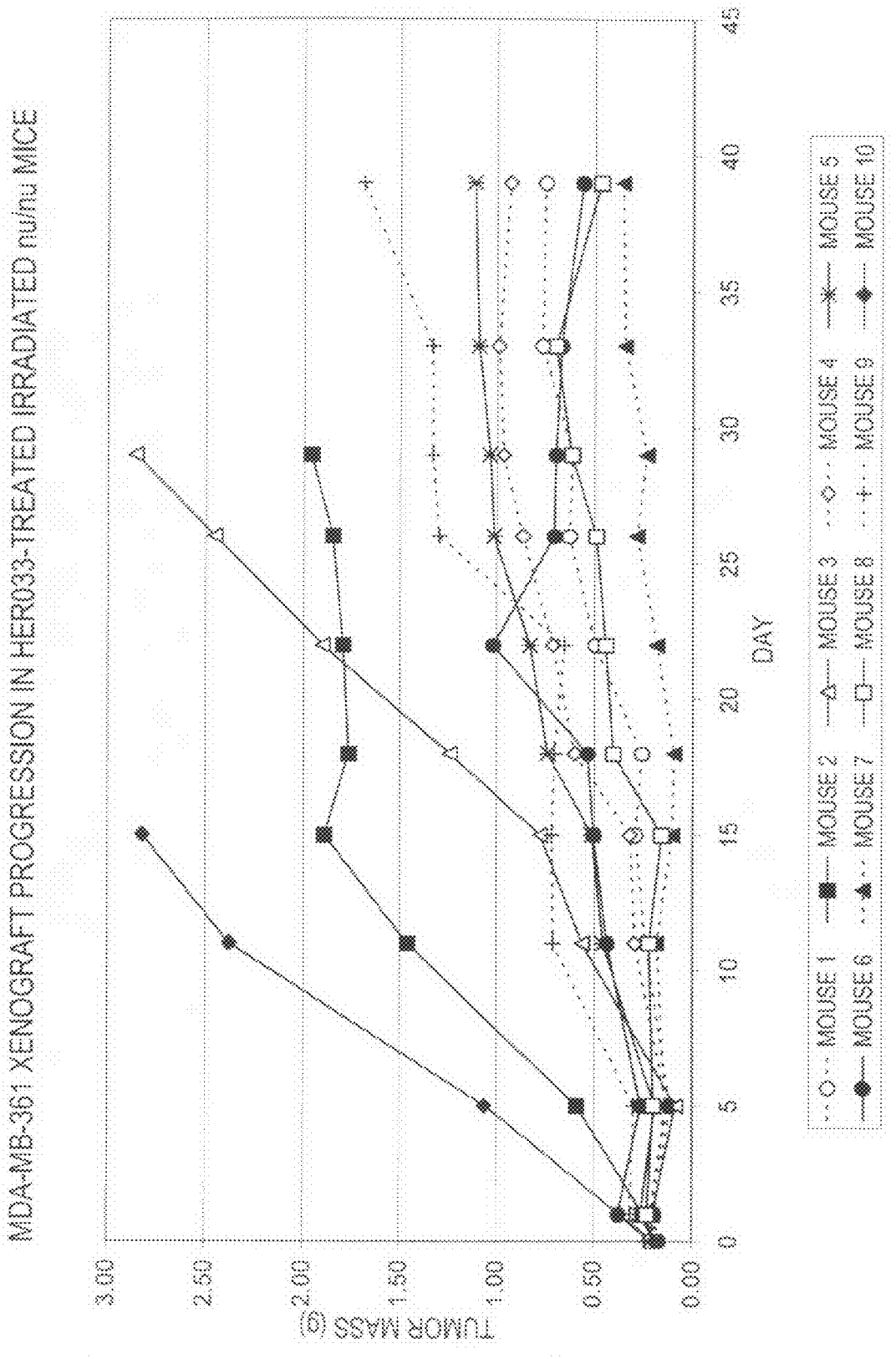

MDA-MB-361 XENOGRAFT PROGRESSION IN HER033-TREATED IRRADIATED nu/nu MICE
TUMOR MASS (g)
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0
5
10
15
20
25
30
35
40
45
DAY
MOUSE 1
MOUSE 2
MOUSE 3
MOUSE 4
MOUSE 5
MOUSE 6
MOUSE 7
MOUSE 8
MOUSE 9
MOUSE 10

Figure 19C

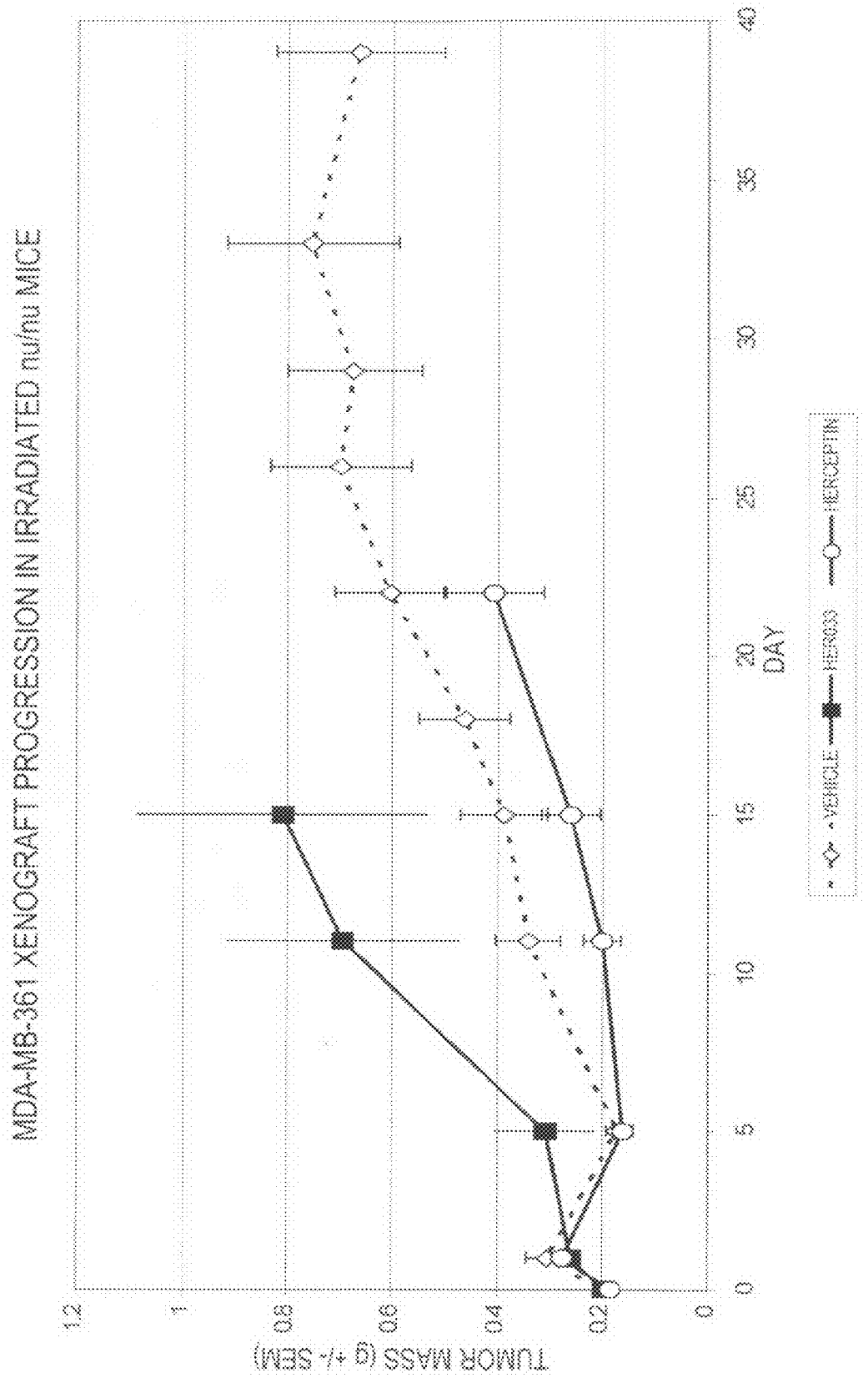

MDA-MB-361 XENOGRAFT PROGRESSION IN IRRADIATED nu/nu MICE
TUMOR MASS (g +/- SEM)
1.2
1
0.8
0.6
0.4
0.2
0
0
5
10
15
20
25
30
35
40
DAY
VEHICLE
HERCEPTIN

Figure 19D

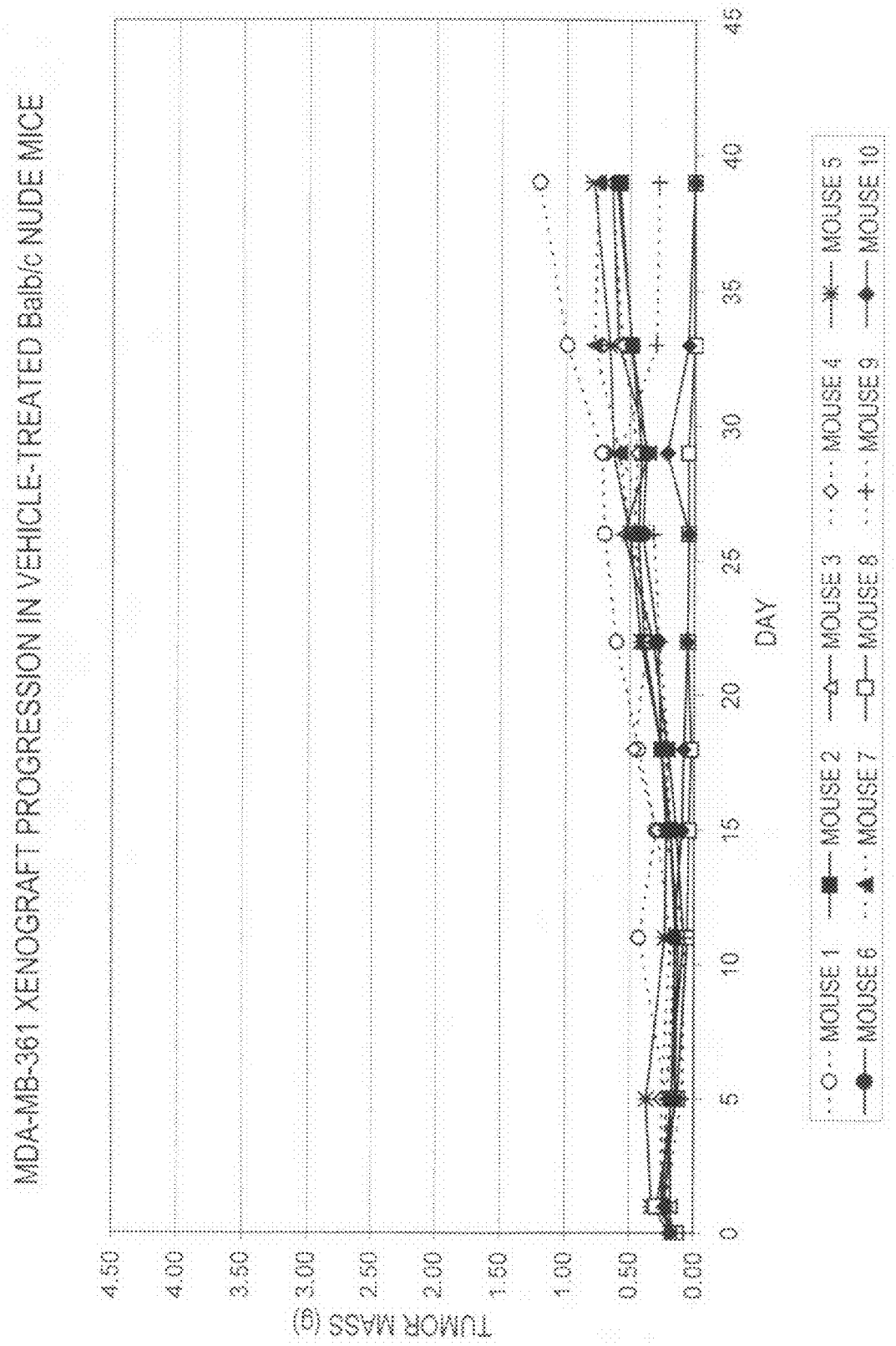

MDA-MB-361 XENOGRAFT PROGRESSION IN VEHICLE-TREATED Balb/c NUDE MICE
TUMOR MASS (g)
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0
5
10
15
20
25
30
35
40
45
DAY
MOUSE 1
MOUSE 2
MOUSE 3
MOUSE 4
MOUSE 5
MOUSE 6
MOUSE 7
MOUSE 8
MOUSE 9
MOUSE 10

Figure 20A

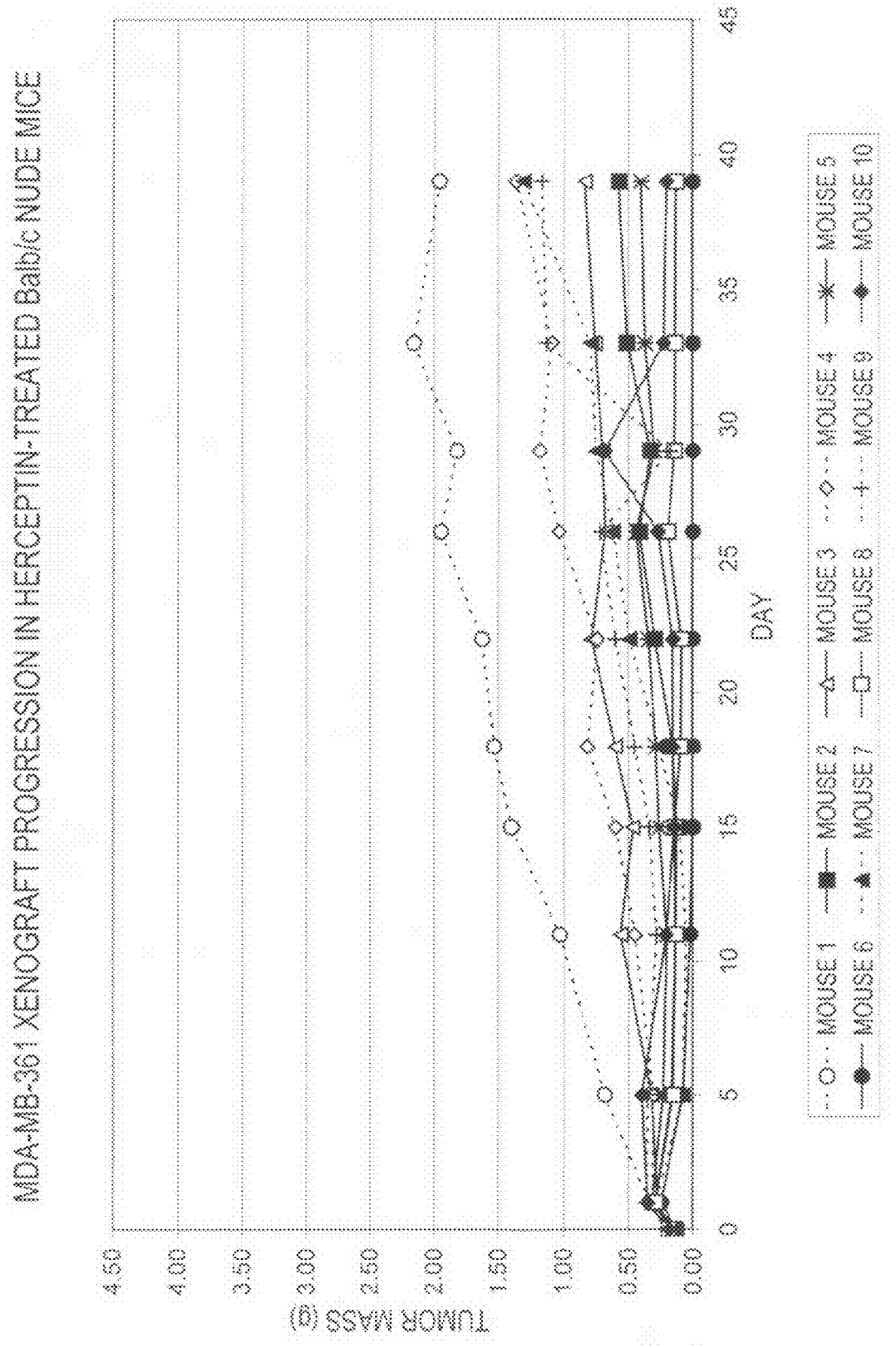

MDA-MB-361 XENOGRAFT PROGRESSION IN HERCEPTIN-TREATED Balb/c NUDE MICE
TUMOR MASS (g)
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0
5
10
15
20
25
30
35
40
45
DAY
MOUSE 1
MOUSE 2
MOUSE 3
MOUSE 4
MOUSE 5
MOUSE 6
MOUSE 7
MOUSE 8
MOUSE 9
MOUSE 10

Figure 20B

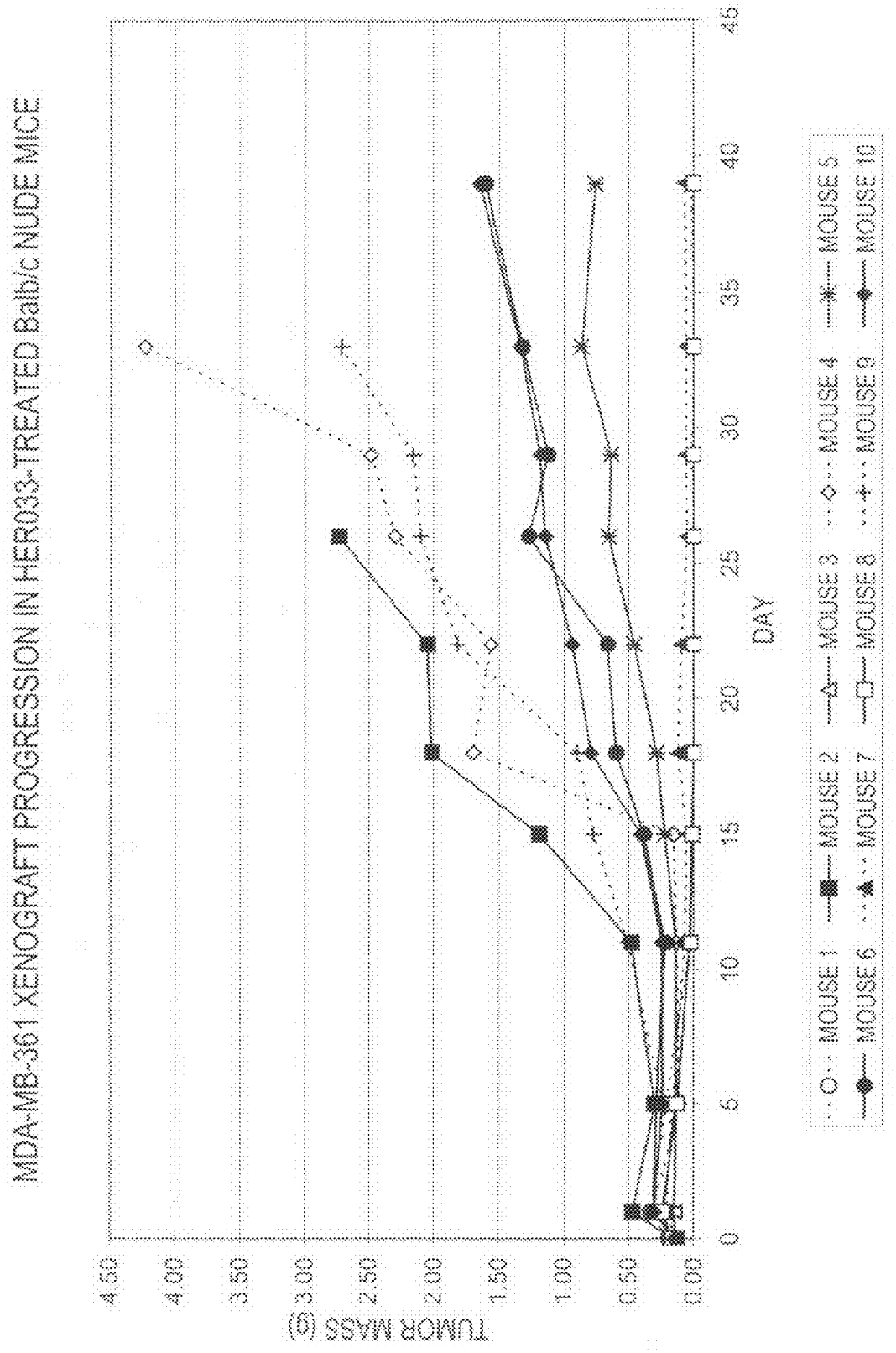

MDA-MB-361 XENOGRAFT PROGRESSION IN HER033-TREATED Balb/c NUDE MICE
TUMOR MASS (g)
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
0
5
10
15
20
25
30
35
40
45
DAY
MOUSE 1
MOUSE 2
MOUSE 3
MOUSE 4
MOUSE 5
MOUSE 6
MOUSE 7
MOUSE 8
MOUSE 9
MOUSE 10

Figure 20C

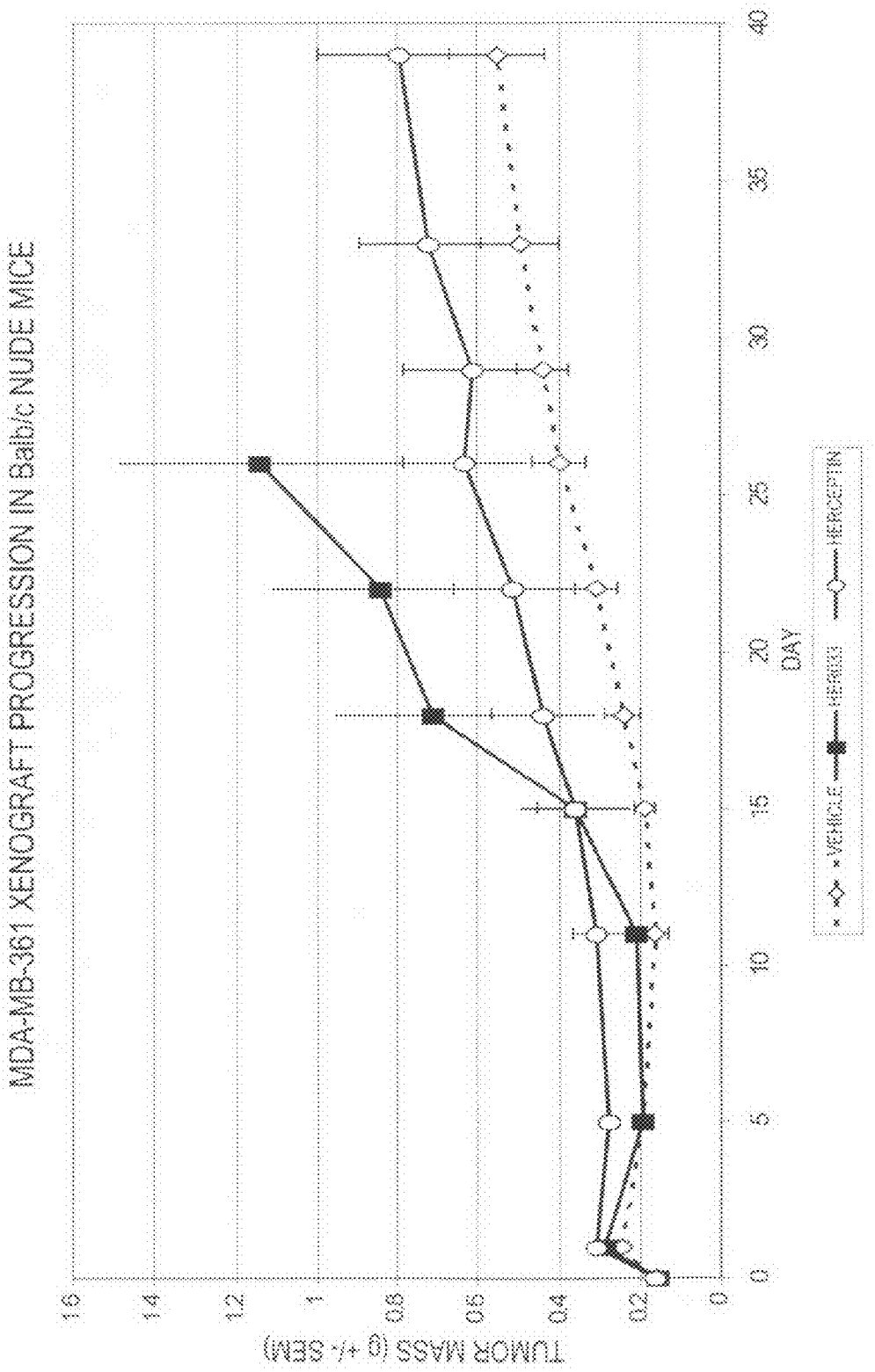

MDA-MB-361 XENOGRAFT PROGRESSION IN Balb/c NUDE MICE
TUMOR MASS (0 +/- SEM)
DAY
VEHICLE
HERCEPTIN

Figure 20D

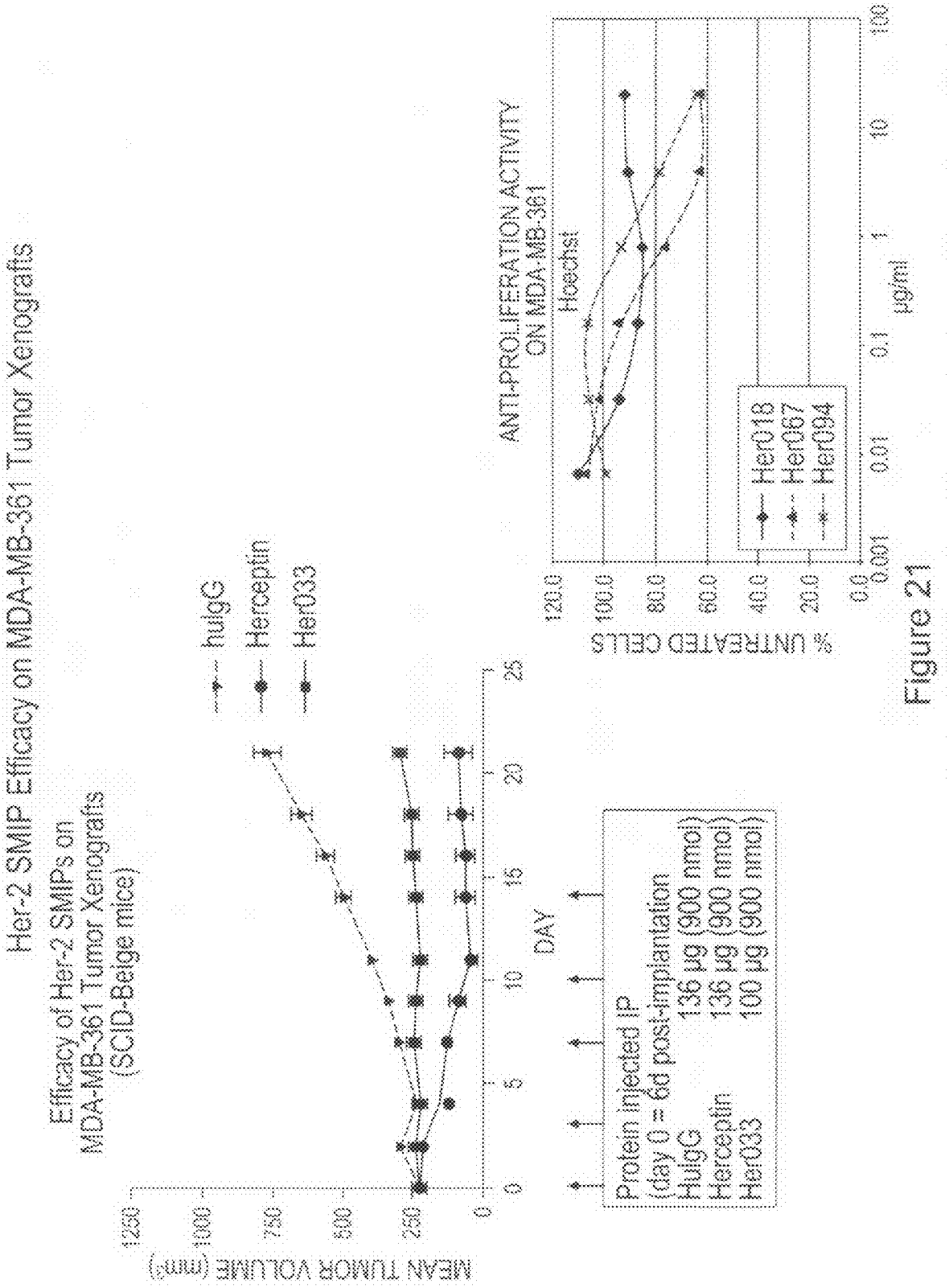

Her-2 SMIP Efficacy on MDA-MB-361 Tumor Xenografts
Efficacy of Her-2 SMIPs on
MDA-MB-361 Tumor Xenografts
(SCID-Beige mice)
huIgG
Herceptin
Her033
MEAN TUMOR VOLUME (mm³)
1250
1000
750
500
250
0
0
5
10
15
20
25
DAY
Protein injected IP
(day 0 = 6d post-implantation
HuIgG 136 µg (900 nmol)
Herceptin 136 µg (900 nmol)
Her033 100 µg (900 nmol)
ANTI-PROLIFERATION ACTIVITY
ON MDA-MB-361
Hoechst
% UNTREATED CELLS
120.0
100.0
80.0
60.0
40.0
20.0
0.0
0.001
0.01
0.1
1
10
100
µg/ml
Her018
Her067
Her094

Figure 21

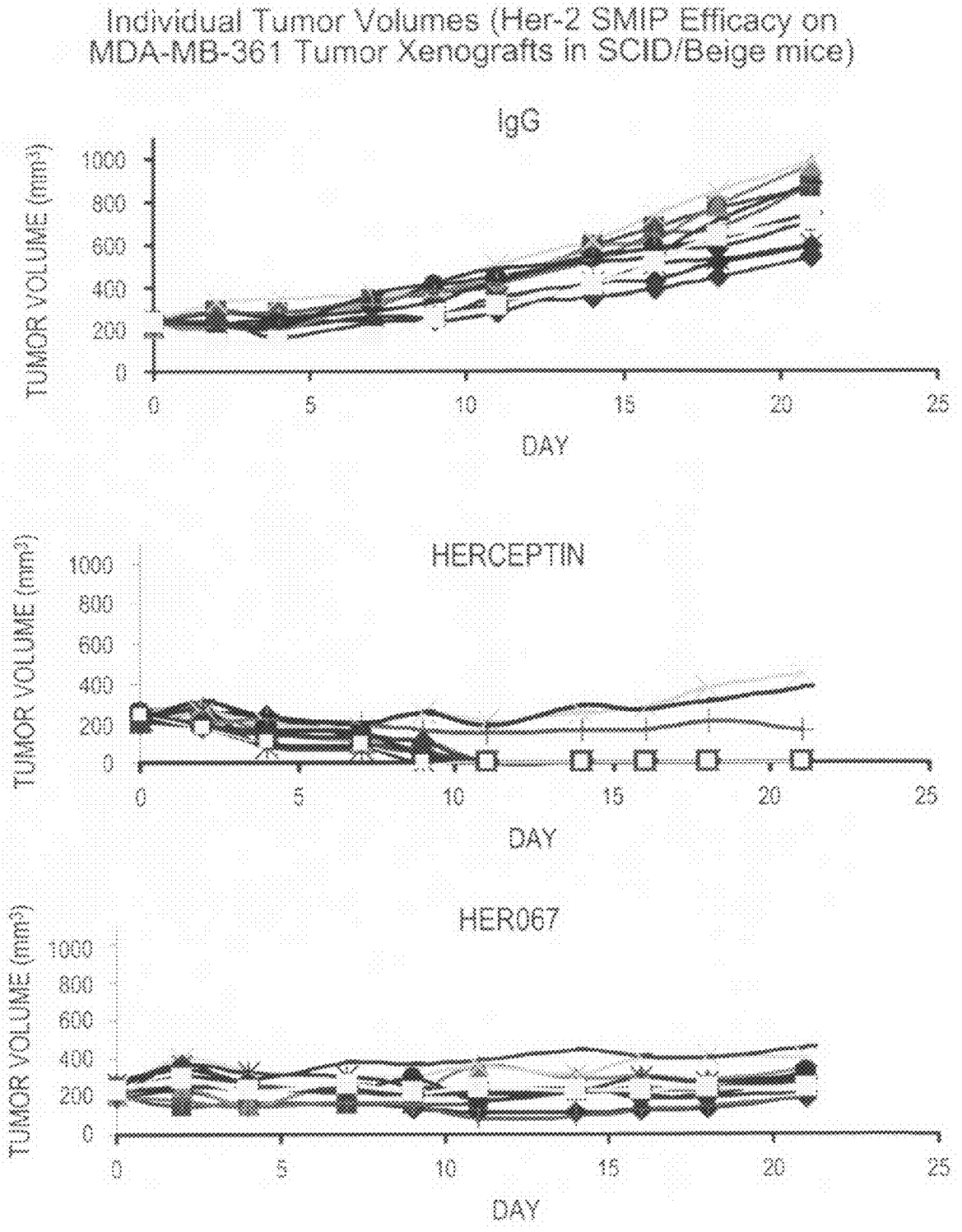

Individual Tumor Volumes (Her-2 SMIP Efficacy on MDA-MB-361 Tumor Xenografts in SCID/Beige mice)
IgG
TUMOR VOLUME (mm³)
1000
800
600
400
200
0
0
5
10
15
20
25
DAY
HERCEPTIN
TUMOR VOLUME (mm³)
1000
800
600
400
200
0
0
5
10
15
20
25
DAY
HER067
TUMOR VOLUME (mm³)
1000
800
600
400
200
0
0
5
10
15
20
25
DAY

Figure 22

THERAPEUTIC COMPOSITIONS AND METHODS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Ser. No. 60/932,302, filed May 29, 2007.

FIELD OF THE INVENTION

[0002] This invention relates to binding proteins that bind erythroblastic leukemia viral oncogene homolog 2 (ErbB2), in particular, human ErbB2 (also known as HER2), and their use in regulating ErbB2-associated activities. The binding proteins disclosed herein are useful in diagnosing, preventing, and/or treating ErbB2 associated disorders, e.g., hyperproliferative disorders, including cancer, and autoimmune disorders, including arthritis.

BACKGROUND OF THE INVENTION

[0003] The ErbB family of receptor tyrosine kinases are important mediators of cell growth, differentiation and survival. The receptor family includes four distinct members including epidermal growth factor receptor (EGFR or ErbB1), HER2 (ErbB2 or $p185^{neu}$), HER3 (ErbB3) and HER4 (ErbB4 or tyro2). Structurally, the ErbB receptors possess an extracellular domain (with four subdomains, I-IV), a single hydrophobic transmembrane domain, and (except for HER3) a highly conserved tyrosine kinase domain. Crystal structures of EGFR reveal a receptor that adopts one of two conformations. In the "closed" conformation, EGFR is not bound by ligand and the extracellular subdomains II and IV remain tightly apposed, preventing inter-receptor interactions. Ligand binding prompts the receptor to adopt an "open" conformation, in which the EGFR receptor is poised to make inter-receptor interactions.

[0004] The ErbB receptors are generally found in various combinations in cells and heterodimerization is thought to increase the diversity of cellular responses to a variety of ErbB ligands. EGFR is bound by at least six different ligands; epidermal growth factor (EGF), transforming growth factor alpha (TGF-α), amphiregulin, heparin binding epidermal growth factor (HB-EGF), betacellulin and epiregulin. A family of heregulin proteins resulting from alternative splicing of a single gene are ligands for ErbB3 and ErbB4. The heregulin family includes alpha, beta and gamma heregulins, neu differentiation factors (NDFs), glial growth factors (GGFs); acetylcholine receptor inducing activity (ARIA); and sensory and motor neuron derived factor (SMDF).

[0005] HER2 was originally identified as the product of the transforming gene from neuroblastomas of chemically treated rats. The activated form of the neu proto-oncogene results from a point mutation (valine to glutamic acid) in the transmembrane region of the encoded protein. Amplification of the human homolog of neu is observed in breast and ovarian cancers and correlates with a poor prognosis. Overexpression of ErbB2 (frequently but not uniformly due to gene amplification) has also been observed in other carcinomas including carcinomas of the stomach, endometrium, salivary gland, lung, kidney, colon, thyroid, pancreas and bladder.

[0006] HER2 has been suggested to be a ligand orphan receptor. Ligand-dependent heterodimerization between HER2 and another HER family member, HER1, HER3 or HER4, activates the HER2 signaling pathway. The intracellular signaling pathway of HER2 is thought to involve ras-MAPK and PI3K pathways, as well as MAPK-independent S6 kinase and phospholipase C-gamma signaling pathways. HER2 signaling also effects proangiogenic factors, vascular endothelial growth factor (VEGF) and interleukin-8 (IL-8), and an antiangiogenic factor, thrombospondin-1 (TSP-1).

[0007] The full-length ErbB2 receptor undergoes proteolytic cleavage releasing its extracellular domain (ECD), which can be detected in cell culture medium and in patient's sera. The truncated ErbB2 receptor (p95ErbB2) that remains after proteolytic cleavage exhibits increased autokinase activity and transforming efficiency compared with the full-length receptor, implicating the ErbB2 ECD as a negative regulator of ErbB2 kinase and oncogenic activity.

[0008] A recombinant humanized version of the murine anti-ErbB2 antibody 4D5 (huMAb4D5-8, rhuMAb HER2 or HERCEPTIN®; U.S. Pat. No. 5,821,337) is clinically active in patients with ErbB2-overexpressing metastatic breast cancers that have received extensive prior anti-cancer therapy (Baselga et al., J. Clin. Oncol. 14:737-744 (1996)). HERCEPTIN® reportedly targets the C-terminal region of domain IV of ErbB2. HERCEPTIN® clinical activity is predominately dependent on antibody dependent cell mediated cytotoxicity (ADCC). Studies have suggested that HERCEPTIN® acts by triggering G1 cell cycle arrest. Presently ErbB-directed therapeutics do not meet the current medical needs. ErbB-directed therapeutics have had only modest anti-tumor efficacy and are not as potent as anticipated from preclinical models. In most patients who initially respond to HERCEPTIN®, disease progression is noted within 1 year. In the metastatic setting, a median duration of roughly nine months was reported, at which point it appears that patients frequently become refractory to therapy. Studies have suggested that more complete blockade of the ErbB receptor family would be beneficial. As there are multiple functional domains of HER2, agents targeted to each of the domains could be a potentially valuable therapeutic. Additionally, there are harmful side effects of HERCEPTIN® treatment. Cardiac dysfunction, quantitated as a decrease in left ventricular ejection fraction (LVEF) of 10% from baseline or less than 50% total, was identified in roughly 7.1% of patients receiving HERCEPTIN® for 1 year versus 2.2% in patients randomized to observation in the HERA trial. Rates of severe and symptomatic congestive heart failure (CHF) were also significantly higher in the group randomized to HERCEPTIN®. Potentially, agents targeting a different HER2 epitopes could avoid these side effects. Accordingly, there remains an urgent need for agents targeting HER2.

[0009] The EGFR family of receptor tyrosine kinases are important regulators of cell growth and proliferation. One member of the family, ErbB2, has been implicated in a host of disorders and diseases including many forms of cancer.

[0010] Accordingly, there is an urgent need for therapeutic and diagnostic agents for detecting and treating ErbB2-mediated disorders including proliferative disorders.

SUMMARY OF THE INVENTION

[0011] The invention relates to novel ErbB2 binding proteins that bind the extracellular domain (ECD) of ErbB2, in particular, human ErbB2. The novel binding protein can be antibody, an antigen-binding fragment of an antibody or a small modular immunopharmaceutical (SMIP). In various embodiments, the binding proteins: bind the ECD in the L1, CR1, L2 or CR2 domain, are ErbB2 agonists, increase

tyrosine phosphorylation of ErbB2 and/or of AKT, MAP kinase (MAPK) or ERK 1/2, preferentially bind ErbB2 ECD homodimer over monomer or shed ECD, reduces ErbB2 mediated proliferation of cancer cells, increase apoptosis in cancer cells, increase the number of cells in S phase after treatment with the binding protein and reduce tumor growth in vivo, or any combination of these properties.

[0012] The invention further relates to nucleic acids encoding the binding proteins or their components, vectors and host cells comprising the nucleic acids and methods of producing the binding proteins by expressing them in the host cells.

[0013] In a further aspect, the invention provides kits and compositions comprising one or more binding proteins of the invention and in some embodiments, further comprising an additional component that is a therapeutic or diagnostic agent, particularly a chemotherapeutic agent.

[0014] The invention also provides methods for producing and identifying binding proteins of the invention and methods for using them, including for treating cancer or other ErbB2 mediated disorders in a subject in need thereof, for reducing proliferation of and/or increasing apoptosis in ErbB2 expressing cells, including cancer cells, for reducing tumor growth and for diagnostic uses, including detecting and/or quantifying the presence of ErbB2 or cells expressing it.

BRIEF DESCRIPTION OF THE FIGURES

[0015] FIG. **1**. Schematic representation of the selection strategy used in the generation of human anti-Her2 scFv binding domains.

[0016] FIG. **2** (A-M). Alignments of the heavy chain amino acid sequences of human anti-Her2 scFvs with the germline human V_H gene sequence. CDRs are in bold type.

[0017] FIG. **3** (A-L). Alignments of the light chain amino acid sequences of human anti-Her2 scFvs with the germline human V_κ or V_λ sequence. CDRs are in bold type.

[0018] FIG. **4**. (A) Schematic diagram of the protein constructs used for selection and screening of scFvs and SMIPs that bind to the extracellular domain of Her2. (B) scFvs and SMIPs are binned into 4 distinct groups according to their binding phenotype as determined using the reagents in FIG. **4**A. (* Herceptin contact sites)

[0019] FIG. **5**. ELISA data for scFv binding to Her2. Binding data for phage-expressed scFv binding to Her2-expressing cells is shown on the left side of the table and data for soluble scFv binding to purified Her2 proteins is shown on the right. ELISA data is scored using a range that correlates with binding signal as indicated by –, + etc.

[0020] FIG. **6**. Binding of HER2 SMIPs (HER067 and HER030), HERCEPTIN® (trastuzumab), and a trastuzumab SMIP (HER018) to (A) HER2 dimer; (B) HER2 monomer; and (C) HER2 shed ectodomain found in SKBR3 supernatant.

[0021] FIG. **7**. ELISA and BIACORE® data for HERCEPTIN® (trastuzumab) and SMIPs binding to Her2. Graphs represent binding of HERCEPTIN® (trastuzumab), Her033 or Her030 binding to various Her2 proteins determined by standard ELISA methods. The table represents Kd values for HERCEPTIN® (trastuzumab), Her033, Her030 and Her018 (Herceptin SMIP) binding to various Her2 proteins as detected by BIACORE®.

[0022] FIG. **8** provides a summary of various specific SMIPs, HERCEPTIN® (trastuzumab), and a trastuzumab SMIP (HER018) binding to various HER2 molecules (different sizes and different species, including human, murine, and macaque) as well as binding to several different cancer cell lines.

[0023] FIGS. **9**A-**9**H show cell surface binding of HER2 SMIPs (HER067 and HER094), HERCEPTIN® (trastuzumab), and a trastuzumab SMIP (HER018) to cell lines (A) Ramos ($Her2^-/CD20^+$ control); (B) BT474; (C) 22rv1; (D) MDA-MB-175; (E) MDA-MB-361 (ATCC); (F) MDA-MB-453; (G) MDA-MB-361 (JL); and (H) SKBR3.

[0024] FIG. **10** provides a summary of the anti-proliferative activity of HER033 SMIP and HERCEPTIN® (trastuzumab) on several different cancer cell lines.

[0025] FIG. **11**. Proliferation of MDA-MB-361 cells following treatment with HER030 or HER033. MDA-MB-361 (ATCC) breast cancer cells were plated in 96-well format and treated with 0-10 ug/ml anti-Her2 or control reagents for 72 hr. Cells were washed, fixed, and stained with DAPI. Stained nuclei were counted using Cellomics High Content assay measuring fluorescence at 360 nM.

[0026] FIG. **12** provides a summary of the anti-proliferative activity of various specific SMIPs, HERCEPTIN® (trastuzumab), and a trastuzumab SMIP (HER018) on several different cancer cell lines.

[0027] FIG. **13**. Western blot analysis of effect of Her033 on Her2 receptor phosphorylation (Y1248) following 24 hr treatment of MDA-MB-361 breast cancer cells. Cells were treated in vitro with Her033, HERCEPTIN® (trastuzumab), or a small molecule Her2 kinase inhibitor for 24 hrs either alone or in the presence of heregulin (HRG1 10 ng/ml) activation of Her3. Protein lysates (50 ug/well) were size fractionated by SDS-PAGE, transferred to nitrocellulose and probed with anti-phospho-Her2(Y1248) antibody. Inhibition of the Her2 receptor kinase blocked the endogenous Her2 autophosphorylation at tyrosine 1248 relative to control. Treatment with Herceptin did not significantly modulate receptor phosphorylation whereas treatment with Her033 stimulated Her2 receptor phosphorylation. Western blots were subsequently reprobed with anti-Actin antibody as protein loading control.

[0028] FIG. **14**. Her033 increases downstream phosphoprotein signal transduction in MDA-MB-361 and BT474 breast cancer cells. Cells were plated in 96-well format and treated with anti-Her2 reagents or Heregulin for 10 minutes. Cells were stained with either rabbit anti-pAKT, anti-pERK, anti-pS6K, or anti-p38MAPK antibodies and ALEXA594 labeled secondary antibody and cellular fluorescence quantified by high content (Cellomics) analysis. In both breast cancer cell lines, treatment with Her033 SMIP induces phosphorylation of AKT and ERK proteins similar to treatment with the Her3 ligand Heregulin. MDA-MB-361 cells also demonstrate significant activation of p38MAP kinase.

[0029] FIG. **15**. Kinetic analysis of Her033 stimulated downstream effector phosphorylation in MDA-MB-361 breast cancer cells. Cells were grown in 96-well format and treated with either anti-Her2 reagents or Her3 ligand Heregulin for 10 min to 24 hr as indicated. Cells were stained with either rabbit anti-pAKT, anti-pERK, anti-pS6K, or anti-p38MAPK antibodies and ALEXA594 labeled secondary antibody and cellular fluorescence quantified by high content (Cellomics) analysis. Her033 treatment induces sustained activation of AKT, ERK and p38MAP kinase phosphorylation in this cell line similar in magnitude to levels following stimulation with 10 ng/ml Heregulin.

[0030] FIGS. **16**A and **16**B show level of phosphorylation of ErbB2, and ERK1/2 in MDA-MB-361 cells when treated with HER2 SMIP HER067, HERCEPTIN® (trastuzumab), and a trastuzumab SMIP (HER018).

[0031] FIG. **17** shows the effect on cell cycle of HER033 SMIP, HERCEPTIN® (trastuzumab), and heregulin on the SKBR3 and BT474 cell lines.

[0032] FIG. **18** shows the effect on cell cycle of HER033 SMIP, HERCEPTIN® (trastuzumab), and heregulin on the MDA-MB-453 and MDA-MB-361 cell lines.

[0033] FIG. **19**. MDA-MB-361 xenograft progression in irradiated nu/nu mice. Female nu/nu mice were exposed to 400 rads of total body irradiation. After three days, they were injected subcutaneously in the dorsal right flank with 1×10^7 MDA-MB-361 cells in Matrigel. When the tumors had reached a mass of 0.1-0.25 g, animals were dosed with Herceptin, HER033, or vehicle (100 ug/mouse, intraperitoneally) on days 1, 4, 6, 8 and 11 (n=10 mice/treatment group). Tumors were measured, and calculated tumor volumes for individual mice are shown for animals treated with vehicle (A), Herceptin (B), or HER033 (C). Animals developing tumors larger than 2.5 g were sacrificed. The mean tumor volume±SEM are plotted in (D). Means were not calculated for treatment groups in which animals with large tumors had been sacrificed.

[0034] FIG. **20**. MDA-MB-361 xenograft progression in Balb/c nude mice. Male Balb/c nude mice were injected subcutaneously in the dorsal right flank with 1×10^7 MDA-MB-361 cells in Matrigel. When the tumors had reached a mass of 0.1-0.25 g, animals were dosed with HERCEPTIN® (trastuzumab), HER033, or vehicle (100 ug/mouse, intraperitoneally) on days 1, 4, 6, 8 and 11 (n=10 mice/treatment group). Tumors were measured, and calculated tumor volumes for individual mice are shown for animals treated with vehicle (A), HERCEPTIN® (trastuzumab) (B), or HER033 (C). Animals developing tumors larger than 2.5 g were sacrificed. The mean tumor volume±SEM are plotted in (D). Means were not calculated for treatment groups in which animals with large tumors had been sacrificed.

[0035] FIGS. **21** and **22** show the in vivo efficacy of HER2 SMIP HER033/HER067 when used to treat SCID-Beige having a tumor xenograft of MDA-MB-361 cells and the in vitro anti-proliferative activity on MDA-MB-361 cells. The top panel of FIG. **21** shows the mean tumor volume in mice treated with HER033 SMIP, HERCEPTIN® (trastuzumab), or vehicle (IgG) after 21 days. The bottom panel of FIG. **21** shows a titration of anti-proliferative activity of HER2 SMIPs (HER067 and HER094) and trastuzumab SMIP (HER018) on the MDA-MB-361 cells used for xenografting in the mice. FIG. **22** shows the tumor volume of individual mice in each treatment group.

DETAILED DESCRIPTION OF THE INVENTION

I. Definitions

[0036] In order that the present invention may be more readily understood, certain terms are first defined. Additional definitions are set forth throughout the detailed description. The present invention provides novel binding proteins that, specifically bind the extra cellular domain (ECD) of ErbB2, especially human ErbB2. In some embodiments, the binding protein is an antibody or an antigen binding fragment of such antibody that specifically binds the ECD. In other embodiments, the binding protein is a small modular immunopharmaceutical (SMIP).

[0037] The term "antibody" refers to an intact four-chain molecule having 2 heavy chains and 2 light chains, each heavy chain and light chain having a variable domain and a constant domain, or an antigen-binding fragment thereof, and encompasses any antigen-binding domain. In various embodiments, an antibody of the invention may be polyclonal, monoclonal, monospecific, polyspecific, bi-specific, humanized, human, chimeric, synthetic, recombinant, hybrid, mutated, grafted (including CDR grafted), or an in vitro generated antibody.

[0038] The term "antigen-binding fragment" of an antibody that specifically binds the ECD of ErbB2 refers to a portion or portions of the antibody that specifically binds to the ECD. An antigen-binding fragment may comprise all or a portion of an antibody light chain variable region (V_L) and/or all or a portion of an antibody heavy chain variable region (V_H) so long as the portion or portions are antigen-binding. However, it does not have to comprise both. Fd fragments, for example, have two V_H regions and often retain some antigen-binding function of the intact antigen-binding domain. Examples of antigen-binding fragments of an antibody include (1) a Fab fragment, a monovalent fragment having the V_L, V_H, C_L and C_H1 domains; (2) a $F(ab')_2$ fragment, a bivalent fragment having two Fab fragments linked by a disulfide bridge at the hinge region; (3) a Fd fragment having the two V_H and C_H1 domains; (4) a Fv fragment having the V_L and V_H domains of a single arm of an antibody, (5) a dAb fragment (Ward et al., (1989) *Nature* 341:544-546), that has a V_H domain; (6) an isolated complementarity determining region (CDR), and (7) a single chain Fv (scFv). Although the two domains of the Fv fragment, V_L and V_H, are coded for by separate genes, they can be joined, using recombinant methods, by a synthetic linker that enables them to be made as a single protein chain in which the V_L and V_H regions pair to form monovalent molecules (known as single chain Fv (scFv); see e.g., Bird et al. (1988) *Science* 242:423-426; and Huston et al. (1988) *Proc. Natl. Acad. Sci. USA* 85:5879-5883). These antibody fragments are obtained using conventional techniques known to those with skill in the art, and the fragments are evaluated for function in the same manner as are intact antibodies.

[0039] The term "effective amount" refers to a dosage or amount that is sufficient to alter ErbB2 activity, to ameliorate clinical symptoms or achieve a desired biological outcome, e.g., decreased cell growth or proliferation, decreased heterodimerization with another member of the EGF family decreased homodimerization, decrease tumor growth rate or tumor size, increased cell death etc.

[0040] The term "human antibody" includes antibodies having variable and constant region sequences corresponding substantially to human germline immunoglobulin sequences known in the art, including, for example, those described by Kabat et al. (See Kabat, et al. (1991) Sequences of Proteins of Immunological Interest, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242). The amino acid sequences of a human antibody, when aligned with germline immunoglobulin sequences, most closely align with human immunoglobulin sequences. The human antibodies of the invention may include amino acid residues not encoded by human germline immunoglobulin sequences (e.g., mutations introduced by random or site-specific

mutagenesis in vitro or by somatic mutation in vivo). Such non-germline residues may occur in a framework region, a CDR, for example in the CDR3, or in the constant region. A human antibody can have one or more residues, such as any number from 1-15, including all of the integers between 1 and 15, or more, replaced with an amino acid residue that is not encoded by the human germline immunoglobulin sequence. CDRs are as defined by Kabat or in Chothia C, Lesk A M, Canonical structures for the hypervariable regions of immunoglobulins, J Mol Biol. 1987 Aug. 20; 196(4):901-17.

[0041] The phrase "inhibit" or "antagonize" an ErbB2/HER2 activity refers to a reduction, inhibition, or otherwise diminution of at least one activity of ErbB2 due to binding an anti-ErbB2 antibody or antigen binding portion, wherein the reduction is relative to the activity of ErbB2 in the absence of the same antibody or antigen-binding portion. The activity can be measured using any technique known in the art, including, for example, as described in the Examples. Activation of the Her2 receptor tyrosine kinase can be measured by the degree of phosphorylation of key tyrosine residues in the intracellular domain. For example, Tyr1248 is a known site of autophosphorylation and thus is a direct measure of Her2 receptor kinase activity. Typically the degree of phosphorylation can be determined by Western blot analysis probing with anti-phopho-Her2 specific antibodies (eg. Tyr1248, Tyr1139, Tyr1112, Tyr877, Tyr1221/1222). Alternatively, cells can be permeabilized and probed with fluorescently labeled phospho-Her2 antibodies and measured either by flow cytometry or high content (Cellomics) analysis. Additionally, the Her2 receptor can be immunoprecipitated, digested with trypsin protease and the degree of phosphorylation at specific sites within the individual Her2 peptides determined by standard Mass Spec techniques. Inhibition or antagonism does not necessarily indicate a total elimination of the ErbB2 polypeptide biological activity. In some embodiments, the reduction in activity may be about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 85%, 90%, 95% or more, including 100% reduction, i.e., elimination of the activity.

[0042] The term "ErbB2" refers to erythroblastic leukemia viral oncogene homolog 2. In the case of human ErbB2, it also is known as c-erb-B2 or HER2/neu. In some embodiments the ErbB2 may comprise: (1) an amino acid sequence of a naturally occurring mammalian ErbB2 polypeptide (full length or mature form) or a fragment thereof, or a fragment thereof; (2) an amino acid sequence substantially identical to, e.g., at least 85%, 90%, 95%, 96%, 97%, 98%, 99% identical to said amino acid sequence or a fragment thereof; (3) an amino acid sequence that is encoded by a naturally occurring mammalian ErbB2 nucleotide sequence or a fragment thereof, or (4) a nucleotide sequence that hybridizes to the foregoing nucleotide sequence under stringent conditions, e.g., highly stringent conditions.

[0043] HER2 or c-erb-B2 encodes a transmembrane receptor protein of 185 kDa, which is structurally related to the epidermal growth factor receptor1. HER2 protein overexpression is observed in 25%-30% of primary breast cancers and is associated with decreased overall survival and a lowered response to chemotherapy and hormonal therapy, which can continue throughout the course of the disease and drives aggressive tumor growth.

[0044] The term "ErbB2 activity" refers to at least one cellular process initiated or interrupted as a result of ErbB2 binding to a receptor complex comprising ErbB2 and an ErbB receptor family member including ErbB1 (EGFR), ErbB2, ErbB3, ErbB4 or comprising an ErbB ligand such as but not limited to EGF, TGF-alpha, amphiregulin, betacellulin, heparin-binding EGF-like growth factor, GP30 on the cell. ErbB2 activity can be determined using any suitable assay methods, for example, protein overexpression can be determined using immunohistochemistry (IHC) and may also be inferred when HER2 gene amplification is identified using fluorescence in situ hybridization (FISH).

[0045] As used herein, "in vitro generated antibody" refers to an antibody where all or part of the variable region (e.g., at least one CDR) is generated in a non-immune cell selection (e.g., an in vitro phage display, protein chip or any other method in which candidate sequences can be tested for their ability to bind to an antigen). This term excludes sequences generated by genomic rearrangement in an immune cell.

[0046] The term "isolated" refers to a molecule that is substantially free of its natural environment. For instance, an isolated protein is substantially free of cellular material or other proteins from the cell or tissue source from which it was derived. The term also refers to preparations where the isolated protein is sufficiently pure for pharmaceutical compositions; or at least 70-80% (w/w) pure; or at least 80-90% (w/w) pure; or at least 90-95% pure; or at least 95%, 96%, 97%, 98%, 99%, or 100% (w/w) pure.

[0047] The phrase "percent identical" or "percent identity" refers to the similarity between at least two different sequences. This percent identity can be determined by standard alignment algorithms, for example, the Basic Local Alignment Tool (BLAST) described by Altshul et al. ((1990) J. Mol. Biol., 215: 403-410); the algorithm of Needleman et al. ((1970) J. Mol. Biol., 48: 444-453); or the algorithm of Meyers et al. ((1988) Comput. Appl. Biosci., 4: 11-17). A set of parameters may be the Blosum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5. The percent identity between two amino acid or nucleotide sequences can also be determined using the algorithm of E. Meyers and W. Miller ((1989) CABIOS, 4:11-17) that has been incorporated into the ALIGN program (version 2.0), using a PAM120 weight residue table, a gap length penalty of 12 and a gap penalty of 4. The percent identity is usually calculated by comparing sequences of similar length.

[0048] The terms "specific binding" or "specifically binds" refer to forming a complex that is relatively stable under physiologic conditions. Specific binding is characterized by a high affinity and a low to moderate capacity as distinguished from nonspecific binding which usually has a low affinity with a moderate to high capacity. Typically, binding is considered specific when the association constant K_A is higher than 10^6 M^{-1}. The appropriate binding conditions, such as concentration of antibodies, ionic strength of the solution, temperature, time allowed for binding, concentration of a blocking agent (e.g., serum albumin, milk casein), etc., may be optimized by a skilled artisan using routine techniques. An antibody is said to specifically bind an antigen when the K_D is $\leqq$1 mM, preferably $\leqq$100 nM.

[0049] As used herein, the term "stringent" describes conditions for hybridization and washing. Stringent conditions are known to those skilled in the art and can be found in *Current Protocols in Molecular Biology*, John Wiley & Sons, N.Y. (1989), 6.3.1-6.3.6. Aqueous and nonaqueous methods are described in that reference and either can be used. One example of stringent hybridization conditions is hybridiza-

tion in 6× sodium chloride/sodium citrate (SSC) at about 45° C., followed by at least one wash in 0.2×SSC, 0.1% SDS at 50° C. A second example of stringent hybridization conditions is hybridization in 6×SSC at about 45° C., followed by at least one wash in 0.2×SSC, 0.1% SDS at 55° C. Another example of stringent hybridization conditions is hybridization in 6×SSC at about 45° C., followed by at least one wash in 0.2×SSC, 0.1% SDS at 60° C. A further example of stringent hybridization conditions is hybridization in 6×SSC at about 45° C., followed by at least one wash in 0.2×SSC, 0.1% SDS at 65° C. High stringent conditions include hybridization in 0.5M sodium phosphate, 7% SDS at 65° C., followed by at least one wash at 0.2×SSC, 1% SDS at 65° C.

[0050] The phrase "substantially as set out," "substantially identical" or "substantially homologous" means that the relevant amino acid or nucleotide sequence (e.g., CDR(s), V_H, or V_L domain) will be identical to or have insubstantial differences (through conserved amino acid substitutions) in comparison to the sequences that are set out. Insubstantial differences include minor amino acid changes, such as 1 or 2 substitutions in a 5 amino acid sequence of a specified region. In the case of antibodies, the second antibody has the same specificity and has at least 50% of the affinity of the first antibody.

[0051] Sequences substantially identical or homologous (e.g., at least about 85% sequence identity) to the sequences disclosed herein are also part of this application. In some embodiment, the sequence identity can be about 85%, 90%, 95%, 96%, 97%, 98%, 99% or higher. Alternatively, substantial identity or homology exists when the nucleic acid segments will hybridize under selective hybridization conditions (e.g., highly stringent hybridization conditions), to the complement of the strand. The nucleic acids may be present in whole cells, in a cell lysate, or in a partially purified or substantially pure form.

[0052] The term "therapeutic agent" is a substance that treats or assists in treating a medical disorder. Therapeutic agents may include, but are not limited to, anti-proliferative agents, anti-cancer agents including chemotherapeutics, antivirals, anti-infectives, immune modulators, and the like that modulate immune cells or immune responses in a manner that complements the ErbB2 activity of an anti-ErbB2 binding protein of the invention. Non-limiting examples and uses of therapeutic agents are described herein.

[0053] As used herein, a "therapeutically effective amount" of an anti-ErbB2 binding protein refers to an amount of an binding protein that is effective, upon single or multiple dose administration to a subject (such as a human patient) at treating, preventing, curing, delaying, reducing the severity of, and/or ameliorating at least one symptom of a disorder or recurring disorder, or prolonging the survival of the subject beyond that expected in the absence of such treatment.

[0054] The term "treatment" refers to a therapeutic or preventative measure. The treatment may be administered to a subject having a medical disorder or who ultimately may acquire the disorder, in order to prevent, cure, delay, reduce the severity of, and/or ameliorate one or more symptoms of a disorder or recurring disorder, or in order to prolong the survival of a subject beyond that expected in the absence of such treatment.

II. Anti-ErbB2 Binding Proteins

[0055] In a first aspect, the invention provides novel ErbB2/HER2, particularly human ErbB2/HER2, ErbB2/HER2 binding proteins that bind in the extra-cellular domain (ECD). In various embodiments, the binding proteins of the invention bind in the LR1, CR1, LR2 or CR2 domain of the ECD. Unlike HERCEPTIN®, in some embodiments the binding proteins of the invention preferentially bind ErbB2 nomodimers over monomers or shed ECD. In some embodiments, the binding proteins of the invention bind ECD homodimers substantially more than monomers. In some cases, the binding protein has no appreciable or significant binding to ECD monomers or to shed ECD.

[0056] In some embodiments, the novel binding proteins are ErbB2 agonists and increase tyrosine phosphorylation of ErbB2, and at the same time, have anti-proliferative activity and pro-apoptotic activity.

[0057] The anti-ErbB2/HER2 binding proteins of the invention can be obtained by any of numerous methods known to those skilled in the art. For example, antibodies can be produced using recombinant DNA methods (U.S. Pat. No. 4,816,567). Monoclonal antibodies may be produced by generation of hybridomas (see e.g., Kohler and Milstein (1975) *Nature,* 256: 495-499) in accordance with known methods. Hybridomas formed in this manner are then screened using standard methods, such as enzyme-linked immunosorbent assay (ELISA) and surface plasmon resonance (BIACORE™) analysis, to identify one or more hybridomas that produce an antibody that specifically binds with a specified antigen. Any form of the specified antigen may be used as the immunogen, e.g., recombinant antigen, naturally occurring forms, any variants or fragments thereof, as well as antigenic peptide thereof.

[0058] One exemplary method of making antibodies includes screening protein expression libraries, e.g., phage or ribosome display libraries. Phage display is described, for example, in Ladner et al., U.S. Pat. No. 5,223,409; Smith (1985) *Science* 228:1315-1317; Clackson et al. (1991) *Nature,* 352: 624-628; Marks et al. (1991) *J. Mol. Biol.,* 222: 581-597WO 92/18619; WO 91/17271; WO 92/20791; WO 92/15679; WO 93/01288; WO 92/01047; WO 92/09690; and WO 90/02809.

[0059] In addition to the use of display libraries, the specified antigen can be used to immunize a non-human animal, e.g., a rodent, e.g., a mouse, hamster, or rat. In one embodiment, the non-human animal includes at least a part of a human immunoglobulin gene. For example, it is possible to engineer mouse strains deficient in mouse antibody production with large fragments of the human Ig loci. Using the hybridoma technology, antigen-specific monoclonal antibodies derived from the genes with the desired specificity may be produced and selected. See, e.g., XENOMOUSE™, Green et al. (1994) *Nature Genetics* 7:13-21, US 2003-0070185, WO 96/34096, published Oct. 31, 1996, and PCT Application No. PCT/US96/05928, filed Apr. 29, 1996.

[0060] The subunit structures, e.g., a C_H, V_H, C_L, V_L, CDR, FR, and three-dimensional configurations of different classes of immunoglobulins are well known in the art. For a review of the antibody structure, see *Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory*, eds. Harlow et al., 1988. One of skill in the art will recognize that a complete 4-chain immunoglobulin comprises active portions, e.g., a portion of the V_H or V_L domain or a CDR that binds to the antigen, i.e., an antigen-binding fragment, or, e.g., the portion of the C_H subunit that binds to and/or activates, e.g., an Fc receptor and/or complement. CDRs typically refer to regions that are hypervariable in sequence and/or form structurally defined

loops, for example, Kabat CDRs are based on sequence variability, as described in *Sequences of Proteins of Immunological Interest, US Department of Health and Human Services* (1991), eds. Kabat et al, or alternatively, to the location of the hypervariable structural loops as described by Chothia. See, e.g., Chothia, D. et al. (1992) *J. Mol. Biol.* 227:799-817; and Tomlinson et al. (1995) *EMBO J.* 14:4628-4638. Still another standard is the AbM definition used by Oxford Molecular's AbM antibody modelling software, which defines the contact hypervariable regions based on crystal structure. See, generally, e.g., *Protein Sequence and Structure Analysis of Antibody Variable Domains. In: Antibody Engineering Lab Manual* (Ed.: Duebel, S, and Kontermann, R., Springer-Verlag, Heidelberg). Embodiments described with respect to Kabat CDRs can alternatively be implemented using similar described relationships with respect to Chothia hypervariable loops or to the AbM-defined loops.

[0061] In another embodiment, a monoclonal antibody is obtained from the non-human animal, and then modified, e.g., humanized, deimmunized, chimeric, may be produced using recombinant DNA techniques known in the art. A variety of approaches for making chimeric antibodies have been described. See e.g., Morrison et al., *Proc. Natl. Acad. Sci. U.S.A.* 81:6851, 1985; Takeda et al., *Nature* 314:452, 1985, Cabilly et al., U.S. Pat. No. 4,816,567; Boss et al., U.S. Pat. No. 4,816,397; Tanaguchi et al., European Patent Publication EP171496; European Patent Publication 0173494, United Kingdom Patent GB 2177096B. Humanized antibodies may also be produced, for example, using transgenic mice that express human heavy and light chain genes, but are incapable of expressing the endogenous mouse immunoglobulin heavy and light chain genes. Winter describes an exemplary CDR-grafting method that may be used to prepare the humanized antibodies described herein (U.S. Pat. No. 5,225,539). All of the CDRs of a particular human antibody may be replaced with at least a portion of a non-human CDR, or only some of the CDRs may be replaced with non-human CDRs. It is only necessary to replace the number of CDRs required for binding of the humanized antibody to a predetermined antigen.

[0062] Humanized antibodies or fragments thereof can be generated by replacing sequences of the Fv variable domain that are not directly involved in antigen binding with equivalent sequences from human Fv variable domains. Exemplary methods for generating humanized antibodies or fragments thereof are provided by Morrison (1985) *Science* 229:1202-1207; by Oi et al. (1986) *BioTechniques* 4:214; and by U.S. Pat. No. 5,585,089; U.S. Pat. No. 5,693,761; U.S. Pat. No. 5,693,762; U.S. Pat. No. 5,859,205; and U.S. Pat. No. 6,407,213. Those methods include isolating, manipulating, and expressing the nucleic acid sequences that encode all or part of immunoglobulin Fv variable domains from at least one of a heavy or light chain. Such nucleic acids may be obtained from a hybridoma producing an antibody against a predetermined target, as described above, as well as from other sources. The recombinant DNA encoding the humanized antibody molecule can then be cloned into an appropriate expression vector.

[0063] In certain embodiments, a humanized antibody is optimized by the introduction of conservative substitutions, consensus sequence substitutions, germline substitutions and/or backmutations. Such altered immunoglobulin molecules can be made by any of several techniques known in the art, (e.g., Teng et al., *Proc. Natl. Acad. Sci. U.S.A.*, 80: 7308-7312, 1983; Kozbor et al., *Immunology Today*, 4: 7279, 1983; Olsson et al., *Meth. Enzymol.*, 92: 3-16, 1982), and may be made according to the teachings of PCT Publication WO92/06193 or EP 0239400).

[0064] An antibody or fragment thereof may also be modified by specific deletion of human T cell epitopes or "deimmunization" by the methods disclosed in WO 98/52976 and WO 00/34317. Briefly, the heavy and light chain variable domains of an antibody can be analyzed for peptides that bind to MHC Class II; these peptides represent potential T-cell epitopes (as defined in WO 98/52976 and WO 00/34317). For detection of potential T-cell epitopes, a computer modeling approach termed "peptide threading" can be applied, and in addition a database of human MHC class II binding peptides can be searched for motifs present in the V_H and V_L sequences, as described in WO 98/52976 and WO 00/34317. These motifs bind to any of the 18 major MHC class II DR allotypes, and thus constitute potential T cell epitopes. Potential T-cell epitopes detected can be eliminated by substituting small numbers of amino acid residues in the variable domains, or preferably, by single amino acid substitutions. Typically, conservative substitutions are made. Often, but not exclusively, an amino acid common to a position in human germline antibody sequences may be used. Human germline sequences, e.g., are disclosed in Tomlinson, et al. (1992) *J. Mol. Biol.* 227:776-798; Cook, G. P. et al. (1995) *Immunol. Today* Vol. 16 (5): 237-242; Chothia, D. et al. (1992) *J. Mol. Biol.* 227:799-817; and Tomlinson et al. (1995) *EMBO J.* 14:4628-4638. The V BASE directory provides a comprehensive directory of human immunoglobulin variable region sequences (compiled by Tomlinson, I. A. et al. MRC Centre for Protein Engineering, Cambridge, UK). These sequences can be used as a source of human sequence, e.g., for framework regions and CDRs. Consensus human framework regions can also be used, e.g., as described in U.S. Pat. No. 6,300,064.

[0065] In certain embodiments, an antibody can contain an altered immunoglobulin constant or Fc region. For example, an antibody produced in accordance with the teachings herein may bind more strongly or with more specificity to effector molecules such as complement and/or Fc receptors, which can control several immune functions of the antibody such as effector cell activity, lysis, complement-mediated activity, antibody clearance, and antibody half-life. Typical Fc receptors that bind to an Fc region of an antibody (e.g., an IgG antibody) include, but are not limited to, receptors of the FcγRI, FcγRII, and FcγRIII and FcRn subclasses, including allelic variants and alternatively spliced forms of these receptors. Fc receptors are reviewed in Ravetch and Kinet, *Annu. Rev. Immunol* 9:457-92, 1991; Capel et al., *Immunomethods* 4:25-34, 1994; and de Haas et al., *J. Lab. Clin. Med.* 126:330-41, 1995).

[0066] For additional antibody production techniques, see Antibodies: A Laboratory Manual, eds. Harlow et al., Cold Spring Harbor Laboratory, 1988. The present invention is not necessarily limited to any particular source, method of production, or other special characteristics of an antibody.

[0067] In some embodiments, an anti-ErbB2 antibody of the invention may be a V_{HH} molecule. V_{HH} molecules (or nanobodies), as known to the skilled artisan, are heavy chain variable domains derived from immunoglobulins naturally devoid of light chains, such as those derived from Camelidae as described in WO9404678, incorporated herein by reference. Such a VHH molecule can be derived from antibodies raised in Camelidae species, for example in camel, llama,

dromedary, alpaca and guanaco and is sometomes called a camelid or camelized variable domain. See e.g., Muyldermans., *J. Biotechnology* (2001) 74(4):277-302, incorporated herein by reference. Other species besides Camelidae may produce heavy chain antibodies naturally devoid of light chain. V_{HH} molecules are about 10 times smaller than IgG molecules. They are single polypeptides in which the CDR3 is longer than a conventional antibody, the VH:VL interface residues are different, and extra cysteines are generally present. These molecules tend to be very stable, resisting extreme pH and temperature conditions. Moreover, they are resistant to the action of proteases which is not the case for conventional antibodies. Furthermore, in vitro expression of V_{HH}s produces high yield, properly folded functional V_{HH}s. In addition, antibodies generated in Camelids will recognize epitopes other than those recognized by antibodies generated in vitro through the use of antibody libraries or via immunization of mammals other than Camelids (see WO 9749805, that is incorporated herein by reference). In additional embodiments, an anti-ErbB2 antibodies or binding fragments of the invention may include single domain antibodies such as immunoglobulin new antigen receptors (IgNARs), which are a unique group of antibody isotypes found in the serum of sharks (Greenberg et al., Nature 374: 168-173 (1995); Nuttall et al., Mol. Immunol., 38: 313-326. (2001)). These are bivalent molecules, targeting antigen through a single immunoglobulin variable domain (~13 kDa) displaying two complementarity determining region (CDR) loops (Roux et al., Proc. Natl. Acad. Sci., 95: 11804-11809 (1998)) and having unusually long and structurally complex CDR3s, which display a high degree of variability (Greenberg et al., 1995).

[0068] Antibodies, also known as immunoglobulins, are typically tetrameric glycosylated proteins composed of two light (L) chains of approximately 25 kDa each and two heavy (H) chains of approximately 50 kDa each. Two types of light chain, termed lambda and kappa, may be found in antibodies. Depending on the amino acid sequence of the constant domain of heavy chains, immunoglobulins can be assigned to five major classes: A, D, E, G, and M, and several of these may be further divided into subclasses (isotypes), e.g., IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2. Each light chain includes an N terminal variable (V) domain (V_L) and a constant (C) domain (C_L). Each heavy chain includes an N terminal V domain (V_H), three or four C domains (C_Hs), and a hinge region collectively referred to as the constant region of the heavy chain. The C_H domain most proximal to V_H is designated as C_H1. The V_H and V_L domains consist of four regions of relatively conserved sequences called framework regions (FR1, FR2, FR3, and FR4), that form a scaffold for three regions of hypervariable sequences also referred to as complementarity determining regions CDRs. CDRs are referred to as CDR1, CDR2, and CDR3. Accordingly, CDR constituents on the heavy chain may be referred to as HCDR1, HCDR2, and HCDR3, while CDR constituents on the light chain are referred to as LCDR1, LCDR2, and LCDR3. CDR3 is typically the greatest source of molecular diversity within the antibody-binding site.

[0069] The anti-ErbB2 binding proteins of the invention include complete 4-chain antibodies and antigen-binding fragments of complete antibodies. An antigen-binding fragment (also referred to as an antigen-binding portion) includes but is not limited to Fab, Fv and ScFv molecules. The Fab fragment (Fragment antigen-binding) consists of V_H-C_H1 and V_L-C_L domains covalently linked by a disulfide bond between the constant regions. The F_v fragment is smaller and consists of V_H and V_L domains non-covalently linked. To overcome the tendency of non-covalently linked domains to dissociate, a single chain F_v fragment (scF_v) can be constructed. The scFv contains a flexible polypeptide that links (1) the C-terminus of V_H to the N-terminus of V_L, or (2) the C-terminus of V_L to the N-terminus of V_H. Repeating units of (Gly_4Ser)—often 3 or 4 repeats may be used as a linker, but other linkers are known in the art.

[0070] A "bispecific" or "bifunctional antibody" is an artificial hybrid antibody having two different heavy/light chain pairs and two different binding sites. Bispecific antibodies can be produced by a variety of methods including fusion of hybridomas or linking of Fab' fragments. See, e.g., Songsivilai & Lachmann, *Clin. Exp. Immunol.* 79:315-321 (1990); Kostelny et al., *J. Immunol.* 148, 1547-1553 (1992). In one embodiment, the bispecific antibody comprises a first binding domain polypeptide, such as a Fab' fragment, linked via an immunoglobulin constant region to a second binding domain polypeptide.

[0071] In some embodiments, an anti-ErbB2 binding protein of the invention is a Small Modular ImmunoPharmaceuticals (SMIP™). SMIPs and their uses and applications are disclosed in, e.g., U.S. Published Patent Application. Nos. 2003/0118592, 2003/0133939, 2004/0058445, 2005/0136049, 2005/0175614, 2005/0180970, 2005/0186216, 2005/0202012, 2005/0202023, 2005/0202028, 2005/0202534, and 2005/0238646, and related patent family members thereof, all of which are hereby incorporated by reference herein in their entireties.

A SMIP™ typically refers to a binding domain-immunoglobulin fusion protein that includes a binding domain polypeptide that is fused or otherwise connected to an immunoglobulin hinge or hinge-acting region polypeptide, which in turn is fused or otherwise connected to a region comprising one or more native or engineered constant regions from an immunoglobulin heavy chain, other than C_H1, for example, the C_H2 and C_H3 regions of IgG and IgA, or the C_H3 and C_H4 regions of IgE (see e.g., U.S. 2005/0136049 by Ledbetter, J. et al., which is incorporated by reference, for a more complete description). The binding domain-immunoglobulin fusion protein can further include a region that includes a native or engineered immunoglobulin heavy chain C_H2 constant region polypeptide (or C_H3 in the case of a construct derived in whole or in part from IgE) that is fused or otherwise connected to the hinge region polypeptide and a native or engineered immunoglobulin heavy chain C_H3 constant region polypeptide (or C_H4 in the case of a construct derived in whole or in part from IgE) that is fused or otherwise connected to the C_H2 constant region polypeptide (or C_H3 in the case of a construct derived in whole or in part from IgE). Typically, such binding domain-immunoglobulin fusion proteins are capable of at least one immunological activity selected from the group consisting of antibody dependent cell-mediated cytotoxicity, complement fixation, and/or binding to a target, for example, a target antigen, such as human ErbB2.

[0072] The binding domain of a SMIP of the invention may contain a complete V_H and a complete V_L joined by linker antigen-binding portions of a V_H and/or V_L and may V2 or be linked in either orientation, i.e., V_H-linker-V_L or V_L-linker-V_H. Any suitable linker can be used in a SMIP of the invention and will be known to those of skill in the art. Exemplary linkers may be found, for example in WO 2007/146968

Tables 5 and 10-12 of which are incorporated by reference in their entirety. Likewise, any immunoglobulin hinge sequence or hinge-acting sequence may be used in a SMIP of the invention.

[0073] In some SMIP embodiments at least one of the immunoglobulin heavy chain constant region polypeptides (i.e., CH2, CH3 or CH4) is from a human immunoglobulin heavy chain. In various embodiments, the immunoglobulin heavy chain constant region polypeptides are of an isotype selected from human IgG and human IgA. In certain further embodiments of the above described SMIP, the linker polypeptide comprises at least one polypeptide having as an amino acid sequence (Gly_4, Ser) and in certain other embodiments the linker polypeptide comprises at least three repeats of said polypeptide. In certain embodiments the immunoglobulin hinge region polypeptide comprises a human IgA hinge region polypeptide.

[0074] An immunoglobulin hinge region polypeptide, as discussed above, includes any hinge peptide or polypeptide that occurs naturally, as an artificial peptide or as the result of genetic engineering and that is situated in an immunoglobulin heavy chain polypeptide between the amino acid residues responsible for forming intrachain immunoglobulin-domain disulfide bonds in CH1 and CH2 regions; hinge region polypeptides for use in the present invention may also include a mutated hinge region polypeptide. Accordingly, an immunoglobulin hinge region polypeptide may be derived from, or may be a portion or fragment of (i.e., one or more amino acids in peptide linkage, typically 5-65 amino acids, preferably 10-50, more preferably 15-35, still more preferably 18-32, still more preferably 20-30, still more preferably 21, 22, 23, 24, 25, 26, 27, 28 or 29 amino acids) an immunoglobulin polypeptide chain region classically regarded as having hinge function, as described above. But, a hinge region polypeptide for use in the instant invention need not be so restricted and may include amino acids situated (according to structural criteria for assigning a particular residue to a particular domain that may vary, as known in the art) in an adjoining immunoglobulin domain such as a CH1 domain or a CH2 domain, or in the case of certain artificially engineered immunoglobulin constructs, an immunoglobulin variable region domain.

[0075] Wild-type immunoglobulin hinge region polypeptides include any naturally occurring hinge region that is located between the constant region domains, CH1 and CH2, of an immunoglobulin. The wild-type immunoglobulin hinge region polypeptide is preferably a human immunoglobulin hinge region polypeptide, preferably comprising a hinge region from a human IgG immunoglobulin, and more preferably, a hinge region polypeptide from a human IgG1 isotype. As is known to the art, despite the tremendous overall diversity in immunoglobulin amino acid sequences, immunoglobulin primary structure exhibits a high degree of sequence conservation in particular portions of immunoglobulin polypeptide chains, notably with regard to the occurrence of cysteine residues which, by virtue of their sulfyhydryl groups, offer the potential for disulfide bond formation with other available sulfhydryl groups. Accordingly, in the context of the present invention wild-type immunoglobulin hinge region polypeptides may be regarded as those that feature one or more highly conserved (e.g., prevalent in a population in a statistically significant manner) cysteine residues, and in certain preferred embodiments a mutated hinge region polypeptide may be selected that contains zero or one cysteine residue and that is derived from such a wild-type hinge region.

[0076] A mutated immunoglobulin hinge region polypeptide may comprise a hinge region that has its origin in an immunoglobulin of a species, of an immunoglobulin isotype or class, or of an immunoglobulin subclass that is different from that of the CH2 and CH3 domains. For instance, in certain embodiments of the invention, the SMIP may comprise a binding domain polypeptide that is fused to an immunoglobulin hinge region polypeptide comprising a wild-type human IgA hinge region polypeptide, or a mutated human IgA hinge region polypeptide that contains zero or only one cysteine residues, as described herein. Such a hinge region polypeptide may be fused to an immunoglobulin heavy chain CH2 region polypeptide from a different Ig isotype or class, for example an IgG subclass, which in certain preferred embodiments will be the IgG1 subclass.

[0077] In some embodiments, an anti-ErbB2 antibody of the invention is a V_{HH} molecule. V_{HH} molecules (or nanobodies), as known to the skilled artisan, are heavy chain variable domains derived from immunoglobulins naturally devoid of light chains, such as those derived from Camelidae as described in WO9404678, incorporated herein by reference. Such a V_{HH} molecule can be derived from antibodies raised in Camelidae species, for example in camel, llama, dromedary, alpaca and guanaco and is sometomes called a camelid or camelized variable domain. See e.g., Muyldermans., *J. Biotechnology* (2001) 74(4):277-302, incorporated herein by reference. Other species besides Camelidae may produce heavy chain antibodies naturally devoid of light chain. V_{HH} molecules are about 10 times smaller than IgG molecules. They are single polypeptides and very stable, resisting extreme pH and temperature conditions. Moreover, they are resistant to the action of proteases which is not the case for conventional antibodies. Furthermore, in vitro expression of V_{HH}s produces high yield, properly folded functional V_{HH}s. In addition, antibodies generated in Camelids will recognize epitopes other than those recognized by antibodies generated in vitro through the use of antibody libraries or via immunization of mammals other than Camelids (see WO 9749805, that is incorporated herein by reference).

[0078] Amino acid (AA) sequences of illustrative heavy chain variable domains (V_H) and light chain variable domains (V_L) of the anti-ErbB2 antibodies of this invention, are set forth in the attached Sequence Table. Table 1 provides the Sequence Identifiers (SEQ ID Nos) of the V_H and V_L domains. Thirty-one specific embodiments of the antibodies are identified as: S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_1E1, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_1A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, S1R3C1_CS_1B10, S1R3A1_BMV_1F3, S1R3B1_BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11, S1R3B1_BMV_1A10, S1R3A1_CS_1D11, S1R3C1_DP47_1H1, S1R3A1_CS_1B12, S1R3B1_BMV_1H5, S1R3A1_DP47_1A6, S1R3B1_DP47_1E1 and S1R3B1_BMV_1A1.

TABLE 1

HUMAN ANTI-ErbB2 BINDING DOMAINS

	SEQUENCE IDENTIFIER (SEQ ID Nos:) Variable Domain Protein Sequences	
scFv	Heavy	Light
S1R2A_CS_1F7	1	2 and 63
S1R2A_CS_1D11	3	4 and 64
S1R2C_CS_1D3	5 and 65	6 and 66
S1R2C_CS_1H12	7 and 67	8 and 68
S1R2A_CS_1D3	9	10 and 69
S1R3B2_BMV_1E1	11	12 and 70
S1R3C1_CS_1D3	13	14 and 71
S1R3B2_DP47_1E8	15	16 and 72
S1R3B2_BMV_1G2	17	18 and 73
S1R3B2_BMV_1H5	19	20 and 74
S1R3C1_CS_1A6	21	22 and 75
S1R3B2_DP47_1C9	23	24 and 76
S1R3B2_DP47_1E10	25	26 and 77
S1R3C1_CS_1B10	27	28 and 78
S1R3A1_BMV_1F3	29	30 and 79
S1R3B1_BMV_1G11	31	32 and 80
S1R3A1_BMV_1G4	33	34 and 81
S1R3B1_BMV_1H11	35	36 and 82
S1R3A1_CS_1B9	37	38 and 83
S1R3B1_BMV_1H9	39	40 and 84
S1R3A1_CS_1B10	41	42 and 85
S1R3B1_BMV_1C12	43	44 and 86
S1R3C1_BMV_1H11	45	46 and 87
S1R3B1_BMV_1A10	47	48 and 88
S1R3A1_CS_1D11	49	50 and 89
S1R3C1_DP47_1H1	51	52 and 90
S1R3A1_CS_1B12	53	54 and 91
S1R3B1_BMV_1H5	55	56 and 92
S1R3A1_DP47_1A6	57	58 and 93
S1R3B1_DP47_1E1	59	60 and 94
S1R3B1_BMV_1A1	61	62 and 95

[0079] According to the nomenclature used herein, "S1R2A_CS_1F7" indicates clone 1F7 from round 2A of the first selection from the CS library.

[0080] An anti-ErbB2 binding protein of this invention may optionally comprise antibody constant regions or parts thereof. For example, a V_L domain may be attached at its C-terminal end to a light chain constant domain which can be a Cκ or a Cλ. Similarly, a V_H domain or portion thereof may be attached to all or part of a heavy chain constant region, which can be a IgA, IgD, IgE, IgG, or IgM constant region or any isotype subclass including IgG1, IgG2, IgG3, IgG4, IgA1 or IgA2. Constant region sequences are known in the art (see, for example, Kabat et al., Sequences of Proteins of Immunological Interest, No. 91-3242, National Institutes of Health Publications, Bethesda, Md. (1991)). Therefore, binding proteins within the scope of this invention may include V_H and V_L domains, or a portion thereof, combined with constant regions or portions thereof known in the art.

[0081] In certain embodiments of the invention, the ErbB2 binding protein comprises a V_H domain, a V_L domain, or a combination thereof, comprising the V_H or V_L amino acid sequence, respectively, found in any one of S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_1E1, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_1A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, S1R3C1_CS_1B10, S1R3A1_BMV_1F3, S1R3B1_BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11, S1R3B1_BMV_1A10, S1R3A1_CS_1D11, S1R3C1_DP47_1H1, S1R3A1_CS_1B12, S1R3B1_BMV_1H5, S1R3A1_DP47_1A6, S1R3B1_DP47_1E1 and S1R3B1_BMV_1A1. In some embodiments, the V_H and V_L are from the same reference antibody. That is, an anti-ErbB2 binding protein of the invention may comprise both the V_H and V_L amino acid sequence of one of the above-listed antibodies.

[0082] An anti-ErbB2 antibody of the invention may comprise one, two, three, four, five or all six complementarity determining regions (CDRs) from any one of the above-listed antibodies. In some embodiments, an anti-ErbB2 binding protein of the invention comprises the HCDR1, HCDR2 and HCDR3 (heavy chain CDR set), the LCDR1, LCDR2 and LCDR3 (light chain CDR set) or both the heavy chain CDR set and the light chain CDR set of one of the thirty-one antibodies exemplified herein.

[0083] A CDR3 sequence found in any one of the thirty-one specifically exemplified antibodies are encompassed within the scope of this invention. For example, in one embodiment, an anti-ErbB2 binding protein of the invention comprises an HCDR3 amino acid sequence found in any one of S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_1E1, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_1A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, S1R3C1_CS_1B10, S1R3A1_BMV_1F3, S1R3B1_BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11, S1R3B1_BMV_1A10, S1R3A1_CS_1D11, S1R3C1_DP47_1H1, S1R3A1_CS_1B12, S1R3B1_BMV_1H5, S1R3A1_DP47_1A6, S1R3B1_DP47_1E1 or S1R3B1_BMV_1A1.

[0084] In certain embodiments, the V_H and/or V_L domains may be germlined, i.e., the framework regions (FR) of these domains are mutated using conventional molecular biology techniques to match the germline sequence. In other embodiments, the FR sequences remain diverged from the consensus germline sequences.

[0085] In one embodiment, mutagenesis is used to make an antibody more similar to one or more germline sequences. This may be desirable when mutations are introduced into the framework region of an antibody through somatic mutagenesis or through error prone PCR. Germline sequences for the V_H and V_L domains can be identified by performing amino acid and nucleic acid sequence alignments against the VBASE database (MRC Center for Protein Engineering, UK). VBASE is a comprehensive directory of all human germline variable region sequences compiled from over a thousand published sequences, including those in the current releases of the Genbank and EMBL data libraries. In some embodiments, the FR regions of the scFvs are mutated in conformity with the closest matches in the VBASE database and the CDR portions are kept intact.

[0086] In certain embodiments, an anti-ErbB2 binding of this invention specifically binds the same epitope as, competes with or cross-competes with an antibody selected from the group consisting of: S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_1E1, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_1A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, S1R3C1_CS_1B10, S1R3A1_BMV_1F3, S1R3B1_

BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11, S1R3B1_BMV_1A10, S1R3A1_CS_1D11, S1R3C1_DP47_1H1, S1R3A1_CS_1B12, S1R3B1_BMV_1H5, S1R3A1_DP47_1A6, S1R3B1_DP47_1E1 and S1R3B1_BMV_1A1, for binding to ErbB2. In some embodiments, such competing or ErbB2-mediated cross-competing binding protein is an ErbB2 agonist and may further reduce proliferation of a cancer call, reduce the rate of growth of an ErbB2-expressing tumor and/or increases apoptosis in such cells and tumors. In some embodiments, such competing or cross-competing binding proteins bind ErbB2 ECD homo-dimers but do not bind ECD monomers or shed ECD.

[0087] Such antibodies can be identified in a competitive binding assay. One can determine whether an antibody binds to the same epitope or cross competes for binding with a binding protein of the invention antibody by using methods known in the art. In one embodiment, one allows the binding protein of the invention to bind to ErbB2 under saturating conditions and then measures the ability of the test protein to bind to the ECD. If the test antibody is able to bind to the ECD at the same time as the reference binding protein, then the test antibody binds to a different epitope than the reference binding protein. However, if the test protein is not able to bind the to the ECD at the same time, then the test protein binds to the same epitope, an overlapping epitope, or an epitope that is in close proximity to the epitope bound by the binding protein of the invention. This experiment can be performed using ELISA, RIA, BIACORE™, or flow cytometry. To test whether a binding protein cross-competes with another anti-ErbB2 binding protein, one may use the competition method described above in two directions, i.e. determining if the known binder blocks the test binder and vice versa. In a preferred embodiment, the experiment is performed using BIACORE™.

[0088] In one embodiment, the association constant (K_A) of an ErbB2 binding protein of the invention is at least 10^6 M^{-1}. In another embodiment, the association constant of these antibodies for human ErbB2 is at least 10^9 M^{-1}. In other embodiments, the association constant of these antibodies for human ErbB2 is at least 10^{10} M^{-1}, at least 10^{11} M^{-1}, or at least 10^{12} M^{-1}. The binding affinity may be determined using techniques known in the art, such as ELISA, biosensor technology, such as biospecific interaction analysis, or other techniques including those described in this application.

[0089] In addition to sequence homology analyses, epitope mapping (see, e.g., Epitope Mapping Protocols, ed. Morris, Humana Press, 1996), and secondary and tertiary structure analyses can be carried out to identify specific 3D structures assumed by the presently disclosed antibodies and their complexes with antigens. Such methods include, but are not limited to, X-ray crystallography (Engstom (1974) Biochem. Exp. Biol., 11:7-13) and computer modeling of virtual representations of the present antibodies (Fletterick et al. (1986) Computer Graphics and Molecular Modeling, in Current Communications in Molecular Biology, Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y.).

[0090] The invention further provides anti-ErbB2 binding proteins that comprise altered V_H and/or V_L sequence(s) compared to the sequences in Table 1. Such binding proteins may be produced by a skilled artisan using techniques well-known in the art. For example, amino acid substitutions, deletions, or additions can be introduced in FR and/or CDR regions. FR changes are usually designed to improve the stability and immunogenicity of the antibody, while CDR changes are typically designed to increase antibody affinity for its antigen. The changes that increase affinity may be tested by altering CDR sequence and measuring antibody affinity for its target (see Antibody Engineering, 2nd ed., Oxford University Press, ed. Borrebaeck, 1995).

[0091] Antibodies whose CDR sequences differ insubstantially from those found in any one of thirty-one specifically exemplified antibodies are encompassed within the scope of this invention. Typically, this involves substitution of an amino acid with an amino acid having similar charge, hydrophobic, or stereochemical characteristics. More drastic substitutions in FR regions, in contrast to CDR regions, may also be made as long as they do not adversely affect (e.g., reduce affinity by more than 50% as compared to unsubstituted antibody) the binding properties of the binding protein. Substitutions may also be made to germine the binding protein or stabilize the antigen binding site.

[0092] Conservative modifications will produce molecules having functional and chemical characteristics similar to those of the molecule from which such modifications are made. In contrast, substantial modifications in the functional and/or chemical characteristics of the molecules may be accomplished by selecting substitutions in the amino acid sequence that differ significantly in their effect on maintaining (1) the structure of the molecular backbone in the area of the substitution, for example, as a sheet or helical conformation, (2) the charge or hydrophobicity of the molecule at the target site, or (3) the size of the molecule.

[0093] For example, a "conservative amino acid substitution" may involve a substitution of a native amino acid residue with a normative residue such that there is little or no effect on the polarity or charge of the amino acid residue at that position. (See, for example, MacLennan et al., 1998, Acta Physiol. Scand. Suppl. 643:55-67; Sasaki et al., 1998, Adv. Biophys. 35:1-24).

[0094] Desired amino acid substitutions (whether conservative or non-conservative) can be determined by those skilled in the art at the time such substitutions are desired. For example, amino acid substitutions can be used to identify important residues of the molecule sequence, or to increase or decrease the affinity of the molecules described herein. Exemplary amino acid substitutions include, but are not limited to, those set forth in Table 2.

TABLE 2

Amino Acid Substitutions

Original Residues	Exemplary Substitutions	More Conservative Substitutions
Ala (A)	Val, Leu, Ile	Val
Arg (R)	Lys, Gln, Asn	Lys
Asn (N)	Gln	Gln
Asp (D)	Glu	Glu
Cys (C)	Ser, Ala	Ser
Gln (Q)	Asn	Asn
Gly (G)	Pro, Ala	Ala
His (H)	Asn, Gln, Lys, Arg	Arg
Ile (I)	Leu, Val, Met, Ala, Phe, Norleucine	Leu
Leu (L)	Norleucine, Ile, Val, Met, Ala, Phe	Ile
Lys (K)	Arg, 1,4 Diamino-butyric Acid, Gln, Asn	Arg

TABLE 2-continued

Amino Acid Substitutions		
Original Residues	Exemplary Substitutions	More Conservative Substitutions
Met (M)	Leu, Phe, Ile	Leu
Phe (F)	Leu, Val, Ile, Ala, Tyr	Leu
Pro (P)	Ala	Gly
Ser (S)	Thr, Ala, Cys	Thr
Thr (T)	Ser	Ser
Trp (W)	Tyr, Phe	Tyr
Tyr (Y)	Trp, Phe, Thr, Ser	Phe
Val (V)	Ile, Met, Leu, Phe, Ala, Norleucine	Leu

[0095] In certain embodiments, conservative amino acid substitutions also encompass non-naturally occurring amino acid residues that are typically incorporated by chemical peptide synthesis rather than by synthesis in biological systems.

[0096] In one embodiment, the method for making a variant V_H domain comprises adding, deleting, or substituting at least one amino acid in the disclosed V_H domains, and testing the variant V_H domain for ErbB2 binding or modulation of ErbB2 activity.

[0097] An analogous method for making a variant V_L domain comprises adding, deleting, or substituting at least one amino acid in the disclosed V_L domains, and testing the variant V_L domain for ErbB2 binding or modulation of ErbB2 activity.

[0098] A further aspect of the invention provides a method for preparing antibodies or antigen-binding fragments that specifically bind ErbB2. The method comprises:

[0099] (a) providing a starting repertoire of nucleic acids encoding a V_H domain that lacks at least one CDR or contains at least one CDR to be replaced;

[0100] (b) inserting into or replacing the CDR region of the starting repertoire with at least one donor nucleic acid encoding an amino acid sequence as substantially set out herein for a V_H CDR, yielding a product repertoire;

[0101] (c) expressing the nucleic acids of the product repertoire;

[0102] (d) selecting a specific antigen-binding fragment that binds to ErbB2; and

[0103] (e) recovering the specific antigen-binding fragment or nucleic acid encoding it.

[0104] In an analogous method, at least one V_L CDR of the invention is combined with a repertoire of nucleic acids encoding a V_L domain that lacks at least one CDR or contains at least one CDR to be replaced. The at least one V_H or V_L CDR may be a CDR1, a CDR2, a CDR3, or a combination thereof, found in any of the thirty-one specifically exemplified antibodies.

[0105] In one embodiment, the variable domain includes a CDR3 to be replaced or lacks a CDR3 encoding region and the at least one donor nucleic acid encodes a CDR3 amino acid sequence found in any one of SEQ ID Nos:1-62 or substantially as found in such sequence.

[0106] In another embodiment, the variable domain includes a CDR1 to be replaced or lacks a CDR1 encoding region and the at least one donor nucleic acid encodes a CDR1 amino acid sequence found in any one of SEQ ID Nos: 1-62.

[0107] In another embodiment, the variable domain includes a CDR2 to be replaced or lacks a CDR2 encoding region and the at least one donor nucleic acid encodes a CDR2 amino acid sequence found in any one of SEQ ID Nos: 1-62.

[0108] In another embodiment, the variable domain includes a CDR3 to be replaced or lacks a CDR3 encoding region and further comprises a CDR1 to be replaced or lacks a CDR1 encoding region, where the at least one donor nucleic acid encodes a CDR3 a CDR1 amino acid sequence, respectively, found in any one of SEQ ID Nos: 1-62.

[0109] In another embodiment, the variable domain includes a CDR3 to be replaced or lacks a CDR3 encoding region and further comprises a CDR2 to be replaced or lacks a CDR2 encoding region, where the at least one donor nucleic acid encodes a CDR3 or CDR2 amino acid sequence, respectively, found in any one of SEQ ID Nos: 1-62.

[0110] In another embodiment, the variable domain includes a CDR3 to be replaced or lacks a CDR3 encoding region and further comprises a CDR1 and a CDR2 to be replaced or lacks a CDR1 and a CDR2 encoding region, where the at least one donor nucleic acid encodes CDR3, CDR1 or CDR2 amino acid sequence, respectively, found in any one of SEQ ID Nos: 1-62.

[0111] Using recombinant DNA methodology, a disclosed CDR sequence may be introduced into a repertoire of V_H or V_L domains lacking the respective CDR (Marks et al. (Bio-Technology (1992) 10: 779-783). For example, a primer adjacent to the 5' end of the variable domain and a primer to the third FR can be used to generate a repertoire of variable domain sequences lacking CDR3. This repertoire can be combined with a CDR3 of an antibody disclosed herein. Using analogous techniques, portions of a disclosed CDR sequence may be shuffled with portions of CDR sequences from other antibodies to provide a repertoire of antigen-binding fragments that bind ErbB2. Either repertoire can be expressed in a host system such as phage display (described in WO 92/01047 and its corresponding U.S. Pat. No. 5,969,108) so suitable antigen-binding fragments that bind to ErbB2 can be selected.

[0112] A further alternative uses random mutagenesis of a V_H or V_L sequence disclosed herein to generate variant V_H or V_L domains still capable of binding ErbB2. A technique using error-prone PCR is described by Gram et al. (Proc. Nat. Acad. Sci. U.S.A. (1992) 89: 3576-3580).

[0113] Another method uses direct mutagenesis of a V_H or V_L sequence disclosed herein. Such techniques are described by Barbas et al. (Proc. Nat. Acad. Sci. U.S.A. (1994) 91: 3809-3813) and Schier et al. (J. Mol. Biol. (1996) 263: 551-567).

[0114] Also encompassed by the invention is a portion of a variable domain that comprises at least one CDR region substantially as set out herein and, optionally, intervening framework regions from the V_H or V_L domains as set out herein. Variable domains lacking a portion of the N-terminus of the FR1 and/or a portion of the C, terminus of the FR4 are also encompassed by the invention. Additional residues at the N-terminal of the FR1 or C-terminal of the FR4 of the variable domain may not be the same residues found in naturally occurring antibodies. For example, construction of antibodies by recombinant DNA techniques often introduces N- or C-terminal residues from its use of linkers. Some linkers may be used to join variable domains to other variable domains (e.g., diabodies), constant domains, or proteinaceous labels.

[0115] Although the embodiments specifically exemplified herein comprise a "matching" pair of V_H and V_L domains, a skilled artisan will recognize that alternative embodiments

may comprise binding proteins containing only a single CDR from either V_L or V_H domain. Either one of the V_H domain or V_L domain can be used to screen for complementary domains capable of forming a two-domain specific binding protein capable of, binding to ErbB2 ECD. The screening may be accomplished by phage display screening methods using the so-called hierarchical dual combinatorial approach disclosed in WO 92/01047. In this approach, an individual colony containing either a H or L chain clone is used to infect a complete library of clones encoding the other chain (L or H), and the resulting two-chain specific antigen-binding domain is selected in accordance with phage display techniques as described.

[0116] In some alternative embodiments, the anti-ErbB2 binding protein can be linked to a protein (e.g., albumin) by chemical cross-linking or recombinant methods. The disclosed antibodies may also be linked to a variety of nonproteinaceous polymers (e.g., polyethylene glycol, polypropylene glycol, or polyoxyalkylenes) in manners set forth in U.S. Pat. No. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192; or 4,179,337. The binding proteins can be chemically modified by covalent conjugation to a polymer, for example, to increase their half-life in blood circulation. Exemplary polymers and attachment methods are shown in U.S. Pat. Nos. 4,766,106; 4,179,337; 4,495,285; and 4,609,546. Binding proteins of the invention can be modified to alter their glycosylation; that is, at least one carbohydrate moiety can be deleted or added to the binding protein. Deletion or addition of glycosylation sites can be accomplished by changing amino acid sequence to delete or create glycosylation consensus sites, that are well known in the art. Another means of adding carbohydrate moieties is the chemical or enzymatic coupling of glycosides to amino acid residues of the antibody (see WO 87/05330 and Aplin et al. (1981) *CRC Crit. Rev. Biochem.,* 22: 259-306). Removal of carbohydrate moieties can also be accomplished chemically or enzymatically (see Hakimuddin et al. (1987) *Arch. Biochem. Biophys.,* 259: 52; Edge et al. (1981) *Anal. Biochem.,* 118: 131; Thotakura et al. (1987) *Meth. Enzymol.,* 138: 350).

[0117] Methods for altering an antibody constant region are known in the art. Antibodies with altered function (e.g., altered affinity for an effector ligand such as FcR on a cell or the C1 component of complement) can be produced by replacing at least one amino acid residue in the constant portion of the antibody with a different residue (see e.g., EP 388,151 A1, U.S. Pat. No. 5,624,821 and U.S. Pat. No. 5,648,260). Similar types of alterations could be described that if applied to a murine or other species antibody would reduce or eliminate similar functions.

[0118] For example, it is possible to alter the affinity of an Fc region of an antibody (e.g., an IgG, such as a human IgG) for FcR (e.g., Fc gamma R1) or C1q. The affinity may be altered by replacing at least one specified residue with at least one residue having an appropriate functionality on its side chain, or by introducing a charged functional group, such as glutamate or aspartate, or perhaps an aromatic non-polar residue such as phenylalanine, tyrosine, tryptophan or alanine (see e.g., U.S. Pat. No. 5,624,821).

[0119] For example, replacing residue 297 (asparagine) with alanine in the IgG constant region significantly inhibits recruitment of effector cells, while only slightly reducing (about three fold weaker) affinity for Clq (see e.g., U.S. Pat. No. 5,624,821). The numbering of the residues in the heavy chain is that of the EU index (see Kabat et al., 1991 supra). This alteration destroys the glycosylation site and it is believed that the presence of carbohydrate is required for Fc receptor binding. Any other substitution at this site that destroys the glycosylation site is believed to cause a similar decrease in lytic activity. Other amino acid substitutions, e.g., changing any one of residues 318 (Glu), 320 (Lys) and 322 (Lys), to Ala, are also known to abolish Clq binding to the Fc region of IgG antibodies (see e.g., U.S. Pat. No. 5,624,821).

[0120] Modified binding proteins can be produced that have a reduced interaction with an Fc receptor. For example, it has been shown that in human IgG_3, which binds to the human Fc gamma R1 receptor, changing Leu 235 to Glu destroys its interaction with the receptor. Mutations on adjacent or close sites in the hinge link region of an antibody (e.g., replacing residues 234, 236 or 237 with Ala) can also be used to affect antibody affinity for the Fc gamma R1 receptor. The numbering of the residues in the heavy chain is based in the EU index (see Kabat et al., 1991 supra).

[0121] Additional methods for altering the lytic activity of an binding protein, for example, by altering at least one amino acid in the N-terminal region of the C_H2 domain, are described in WO 94/29351 by Morgan et al. and U.S. Pat. No. 5,624,821.

[0122] One of skill in the art will appreciate that the modifications described above are not all-exhaustive, and that many other modifications are obvious to a skilled artisan in light of the teachings of the present disclosure.

[0123] A binding protein of this invention may be tagged with a detectable or functional label. These labels include radiolabels (e.g., ^{131}I or ^{99}Tc), enzymatic labels (e.g., horseradish peroxidase or alkaline phosphatase), and other chemical moieties (e.g., biotin).

[0124] In some embodiments, the invention features a human, monoclonal antibody that specifically binds the ECD, ErbB2, in particular, human ErbB2 and possesses one or more of the following characteristics: (1) it is an in vitro generated antibody (2) it is an in vivo generated antibody (e.g., transgenic mouse system); (3) it binds to ErbB2 with an association constant of at least 10^{12} M^{-1}; (4) it binds to ErbB2 with an association constant of at least 10^{11} M^{-1}; (5) it binds to ErbB2 with an association constant of at least 10^{10} M^{-1}; (6) it binds to ErbB2 with an association constant of at least 10^{9} M^{-1}; (7) it binds to ErbB2 with an association constant of at least 10^{6} M^{-1}; (8) it binds to ErbB2 with a dissociation constant of 500 nM or less; (9) it binds to ErbB2 with a dissociation constant of 10 nM or less; (10) it binds to ErbB2 with a dissociation constant of 150 pM or less; (11) it binds to ErbB2 with a dissociation constant of 60 pM or less.

III. Nucleic Acids, Cloning and Expression Systems

[0125] In another aspect, the invention provides isolated nucleic acids encoding an anti-ErbB2 binding protein of the invention. The nucleic acids may comprise DNA or RNA, and they may be synthetic (completely or partially) or recombinant (completely or partially). Reference to a nucleotide sequence as set out herein encompasses a DNA molecule with the specified sequence, and encompasses a RNA molecule with the specified sequence in which U is substituted for T.

[0126] The invention also contemplates nucleic acids that comprise a coding sequence for a CDR1, CDR2 or CDR3, a frame-work sequence (including FR1, FR2, FR3 and/or FR4), a V_H domain, a V_L domain, or combinations thereof, as disclosed herein, or a sequence substantially identical thereto (e.g., a sequence at least 85%, 90%, 95%, 96%, 97%, 98%,

99% or higher identical thereto, or that is capable of hybridizing under stringent conditions to the sequences disclosed).

[0127] In one embodiment, the isolated nucleic acid has a nucleotide sequence encoding a heavy chain variable region and/or a light chain variable region of an anti-ErbB2 binding protein comprising at least one heavy chain CDR or light chain CDR, respectively, chosen from the CDR amino acid sequences found in SEQ ID Nos:1-62, or a sequence encoding a CDR that differs by one or two amino acids from the CDR sequences set forth herein. In some embodiments, the nucleic acid encodes an anti-ErbB2 binding protein comprising one, two, or all 3 heavy chain CDRs, one, two or all 3 light chain CDRs or all 6 CDRS in any of an specifically exemplified antibody.

[0128] The nucleic acid can encode only the light chain or the heavy chain variable region, or can also encode an antibody light or heavy chain constant region, operatively linked to the corresponding variable region. In one embodiment, the light chain variable region is linked to a constant region chosen from a kappa or a lambda constant region. The light chain constant region may also be a human kappa or lambda type. In another embodiment, the heavy chain variable region is linked to a heavy chain constant region of an antibody isotype chosen from IgG (e.g., IgG_1, IgG_2, IgG_3, IgG_4), IgM, IgA_1, IgA_2, IgD, and IgE. The heavy chain constant region may be an IgG (e.g., an IgG_1) isotype.

[0129] The nucleic acid compositions of the present invention, while often in the native sequence (of cDNA or genomic DNA or mixtures thereof) except for modified restriction sites and the like, may be mutated in accordance with standard techniques to provide gene sequences. For coding sequences, these mutations, may affect amino acid sequence as desired. In particular, nucleotide sequences substantially identical to or derived from native V, D, J, constant, switches and other such sequences described herein are contemplated (where "derived" indicates that a sequence is identical or modified from another sequence).

[0130] In one embodiment, the nucleic acid differs (e.g., differs by substitution, insertion, or deletion) from that of the sequences provided (e.g., as follows: by at least one but less than 10, 20, 30, or 40 nucleotides; at least one but less than 1%, 5%, 10% or 20% of the nucleotides in the subject nucleic acid). Also within the invention are ErbB2 binding proteins encoded by a nucleic acid that hybridizes under stringent conditions to a nucleic acid specifically exemplified herein or to its complement. If necessary for this analysis the sequences should be aligned for maximum homology. "Looped out" sequences from deletions or insertions, or mismatches, are considered differences. The difference may be at a nucleotide (s) encoding a non-essential residue(s), or the difference may be a conservative substitution(s).

[0131] The invention also provides nucleic acid constructs in the form of plasmids, vectors, transcription or expression cassettes, that comprise at least one nucleic acid as described herein as well as a host cell that comprises at least one nucleic acid described herein. Suitable host cells for the expression of a binding protein of the invention well be well known in the art and include mammalian, plant, insects, bacterial or yeast cells.

[0132] Also provided are the methods of making an anti-ErbB2 antibody of the invention that is encoded by the nucleic acid(s) comprising sequence described herein. The method comprises culturing host cells under appropriate conditions to express the protein from the nucleic acid. Following expression and production, the encoded pp may be isolated and/or purified using any suitable technique, then used as appropriate. The method can also include the steps of fusing a nucleic acid encoding a scFv with nucleic acids encoding a Fc portion of an antibody and expressing the fused nucleic acid in a cell. The method can also include a step of germ lining.

[0133] Antigen-binding fragments, V_H and/or V_L domains, and encoding nucleic acid molecules and vectors may be isolated and/or purified from their natural environment, in substantially pure or homogenous form, or, in the case of nucleic acid, free or substantially free of nucleic acid or genes of origin other than the sequence encoding a polypeptide with the require function.

[0134] Systems for cloning and expressing polypeptides in a variety of host cells are known in the art. Cells suitable for producing antibodies are described in, for example, Fernandez et al. (1999) Gene Expression Systems, Academic Press, eds. In brief, suitable host cells include mammalian cells, insect cells, plant cells, yeast cells, or prokaryotic cells, e.g., *E. coli*. Mammalian cells available in the art for heterologous polypeptide expression include lymphocytic cell lines (e.g., NSD), HEK293 cells, Chinese hamster ovary (CHO) cells, COS cells, HeLa cells, baby hamster kidney cells, oocyte cells, and cells from a transgenic animal, e.g., mammary epithelial cell.

[0135] In one embodiment, all or a portion of an anti-ErbB2 antibody selected from S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_1 μl, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_1A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, S1R3C1_CS_1B10, S1R3A1_BMV_1F3, S1R3B1_BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11 or S1R3B1_BMV_1A1 is expressed in HEK293 or CHO cells. In other embodiments, one or more nucleic acids encoding an anti-ErbB2 binding protein of the invention are placed under the control of a tissue-specific promoter (e.g., a mammary specific promoter) and the antibodies are produced in transgenic animals. For example, the antibodies are secreted into the milk of the transgenic animal, such as a transgenic cow, pig, horse, sheep, goat or rodent.

[0136] Suitable vectors may be chosen or constructed to contain appropriate regulatory sequences, including promoter sequences, terminator sequences, polyadenylation sequences, enhancer sequences, marker genes, and other sequences. The vectors may also contain a plasmid or viral backbone. For details, see Sambrook et al., Molecular Cloning: A Laboratory Manual, 2nd ed., Cold Spring Harbor Laboratory Press (1989). Many established techniques used with vectors, including the manipulation, preparation, mutagenesis, sequencing, and transfection of DNA, are described in Current Protocols in Molecular Biology, Second Edition, Ausubel et al. eds., John Wiley & Sons (1992).

[0137] A nucleic acid encoding all or part of an anti-ErbB2 binding protein of the invention may be introduced into a host cell by any readily available means. For eukaryotic cells, suitable transfection techniques may include calcium phosphate, DEAE-Dextran, electroporation, liposome-mediated transfection, and transduction using retrovirus or other viruses, e.g., vaccinia or baculovirus. For bacterial cells, suitable techniques may include calcium chloride transformation, electroporation, and transfection using bacteriophage.

DNA introduction may be followed by a selection method (e.g., drug resistance) to select cells that contain the nucleic acid.

IV. Therapeutic Uses of Anti-ErbB2 Binding Proteins

[0138] Anti-ErbB2 binding proteins of the invention may be ErbB2 agonists or antagonists. An agonist ErbB2 binder of the invention increases HER2 tyrosine phosphorylation in the absence or presence of other HER2 agonists such as Heregulin or Epidermal Growth Factor (EGF). Certain HER2 agonists of the invention increase phosphorylation of HER2 pathway proteins. In some embodiments, the agonist of the invention increase phosphorylation of AKT, MAPK and/or ERK. In some embodiments, the HER2 agonist of the invention decreases proliferation and/or increases cell death of a cancer cell, in vitro and in vivo.

[0139] Anti-ErbB2 binding proteins that act as antagonists to ErbB2 can be used to reduce at least one ErbB2-mediated activity, such as reducing ErbB2-mediated tyrosine phosphorylation, decreased heterodimerization of ErbB2 with other ERBB-family members, decreased ErbB2-mediated cell signalling and decreased growth or proliferation of ErbB2-expressing cells. In one embodiment, anti-ErbB2 binding proteins of the invention are used in a method for decreasing tumor growth, the method comprising contacting an ErbB2 expressing cell with a binding protein of the invention to modulate cell proliferation, cytolytic activity, cytokine secretion, or chemokine secretion.

[0140] Accordingly, the binding proteins of the invention can be used to directly or indirectly inhibit or reduce the activity (e.g., proliferation, differentiation, and/or survival) of cells expressing ErbB2, and, thus, can be used to treat a variety of disorders including hyperproliferative disorders.

[0141] The binding proteins of the invention can be used to treat hyperproliferative disorders associated with activity of ErbB2 by administering the antibodies in an amount sufficient to inhibit or reduce hyperproliferation and/or to increase cell death, such as by apoplosis of ErbB2 expressing cells in a subject and allowing the antibodies to treat or prevent the disorder. ErbB2 is expressed in a number of cancers including, but not limited to, breast, bladder, cervical, ovarian, prostate, testicular, oral, colorectal, lung and pancreatic, cancers and in childhood medulloblastoma, oral squamous cell carcinoma, gastric cancer cholangio carcinoma, osteosarcoma, primary Fallopian tube carcinoma, salivary gland tumors and synovial sarcoma. Binding proteins of the invention may be used to inhibit the progression of neoplasms, e.g. squamous cell carcinomas, basal cell carcinomas, transitional cell papillomas and carcinomas, adenomas, adenocarcinoma. According to the invention, an anti-ErbB2 binding protein of the invention can be administered to a subject in need thereof as part of a regimen that comprises another therapeutic modality, such as surgery or radiation.

V. Combination Therapy

[0142] According to the invention, a composition suitable for pharmaceutical use comprising at least one anti-ErbB2 binding protein further comprises at least one additional therapeutic agent. The therapy is useful for treating ErbB2-mediated pathological conditions or disorders including cancer. The term "in combination" in this context means that the binding protein composition and the additional therapeutic agent are given as part of a treatment regimen. In some embodiments, the anti-ErbB2 binding protein is administered substantially contemporaneously, either simultaneously or sequentially. In some embodiments, in which administration is sequential, at the onset of administration of the second agent, the first of the two agents is still detectable at effective concentrations at the site of treatment. In another embodiment, if given sequentially, at the onset of administration of the second compound, the first of the two compounds is not detectable at effective concentrations at the site of treatment.

[0143] For example, the combination therapy can include at least one anti-ErbB2 binding protein of the invention co-formulated with, co-administered with, or administered as part of the same therapeutic regimen as at least one additional therapeutic agent. The additional agents may include at least but is not limited to mitotic inhibitors, alkylating agents, anti-metabolites, intercalating antibiotics, growth factor inhibitors, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biological response modifiers, antibodies, cytotoxics, antiproliferative agents, kinase inhibitors, angiogenesis inhibitors, growth factor inhibitors, cox-I inhibitors, cox-II inhibitors, radiation, cell cycle inhibitors, enzymes, anti-hormones, statins, and anti-androgens.

[0144] In other embodiments, at least one anti-ErbB2 binding protein can be co-formulated with, and/or co-administered with, at least one anti-inflammatory drug, immunosuppressant, metabolic inhibitor, and enzymatic inhibitor.

[0145] In other embodiments, an anti-ErbB2 antibody can be used in combination with at least one binding protein, such as an antibody, directed at other cancer targets. Another aspect of the present invention accordingly relates to kits for carrying out the administration of the anti-ErbB2 binding protein alone or in combination with other therapeutic agents. In one embodiment, the kit comprises at least one anti-ErbB2 binding protein formulated in a pharmaceutical carrier, and at least one additional therapeutic agent, formulated as appropriate in one or more separate pharmaceutical preparations.

[0146] In one embodiment, the present inventive binding proteins can be administered in combination with (e.g., prior to, concurrently with, or subsequent to) one or more other therapeutic agents. Such therapeutic agents include, for example, cytotoxic agents that inhibit or prevent the function of cells and/or causes destruction of cells. The term is intended to include radioactive isotopes (e.g. I131, I125, Y90 and Re186), chemotherapeutic agents, growth inhibitory agents, cytokine, and toxins such as enzymatically active toxins of bacterial, fungal, plant or animal origin, or fragments thereof.

[0147] Examples of chemotherapeutic agents include alkylating agents such as thiotepa and cyclosphosphamide (CYTOXAN™); alkyl sulfonates such as busulfan, improsulfan and piposulfan; aziridines such as benzodopa, carboquone, meturedopa, and uredopa; ethylenimines and methylamelamines including altretamine, triethylenemelamine, triethylenephosphoramide, triethylenethiophosphaoramide and trimethylolomelamine; nitrogen mustards such as chlorambucil, chlornaphazine, cholophosphamide, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard; nitrosureas such as carmustine, chlorozotocin, fotemustine, lomustine, nimustine, ranimustine; antibiotics such as aclacinomysins, actinomycin, authramycin, azaserine, bleomycins, cactinomycin, calicheamicin, carabicin, caminomycin, carzinophilin, chro-

momycins, dactinomycin, daunorubicin, detorubicin, 6-diazo-5-oxo-L-norleucine, doxorubicin, epirubicin, esorubicin, idarubicin, marcellomycin, mitomycins, mycophenolic acid, nogalamycin, olivomycins, peplomycin, potfiromycin, puromycin, quelamycin, rodorubicin, streptonigrin, streptozocin, tubercidin, ubenimex, zinostatin, zorubicin; anti-metabolites such as methotrexate and 5-fluorouracil (5-FU); folic acid analogues such as denopterin, methotrexate, pteropterin, trimetrexate; purine analogs such as fludarabine, 6-mercaptopurine, thiamiprine, thioguanine; pyrimidine analogs such as ancitabine, azacitidine, 6-azauridine, carmofur, cytarabine, dideoxyuridine, doxifluridine, enocitabine, floxuridine, 5-FU; androgens such as calusterone, dromostanolone propionate, epitiostanol, mepitiostane, testolactone; anti-adrenals such as aminoglutethimide, mitotane, trilostane; folic acid replenisher such as frolinic acid; aceglatone; aldophosphamide glycoside; aminolevulinic acid; amsacrine; bestrabucil; bisantrene; edatraxate; defofamine; demecolcine; diaziquone; elformithine; elliptinium acetate; etoglucid; gallium nitrate; hydroxyurea; lentinan; lonidamine; mitoguazone; mitoxantrone; mopidamol; nitracrine; pentostatin; phenamet; pirarubicin; podophyllinic acid; 2-ethylhydrazide; procarbazine; PSK®; razoxane; sizofuran; spirogermanium; tenuazonic acid; triaziquone; 2,2',2"-trichlorotriethylamine; urethan; vindesine; dacarbazine; mannomustine; mitobronitol; mitolactol; pipobroman; gacytosine; arabinoside ("Ara-C"); cyclophosphamide; thiotepa; taxanes, e.g. paclitaxel (TAXOL®, Bristol-Myers Squibb Oncology, Princeton, N.J.) and docetaxel (TAXOTERE®, Rhône-Poulenc Rorer, Antony, France); chlorambucil; gemcitabine; 6-thioguanine; mercaptopurine; methotrexate; platinum analogs such as cisplatin and carboplatin; vinblastine; platinum; etoposide (VP-16); ifosfamide; mitomycin C; mitoxantrone; vincristine; vinorelbine; navelbine; novantrone; teniposide; daunomycin; aminopterin; xeloda; ibandronate; CPT-11; topoisomerase inhibitor RFS 2000; difluoromethylomithine (DMFO); retinoic acid; esperamicins; capecitabine; and pharmaceutically acceptable salts, acids or derivatives of any of the above. Also included are anti-hormonal agents that act to regulate or inhibit hormone action on tumors such as anti-estrogens including for example tamoxifen, raloxifene, aromatase inhibiting 4(5)-imidazoles, 4-hydroxytamoxifen, trioxifene, keoxifene, LY117018, onapristone, and toremifene (Fareston); and anti-androgens such as flutamide, nilutamide, bicalutamide, leuprolide, and goserelin; and pharmaceutically acceptable salts, acids or derivatives of any of the above.

[0148] A growth inhibitory agent when used herein refers to a compound or composition that inhibits growth of a cell, especially an ErbB2-overexpressing cancer cell either in vitro or in vivo. In the context of the present invention, the growth inhibitory agent can be one that significantly reduces the percentage of ErbB2 overexpressing cells in S phase and the binding proteins of the present invention may potentially sensitize the cells to such an S phase agent. S-phase blockers include the vincas (vincristine and vinblastine), taxol, and topo II inhibitors such as doxorubicin, daunorubicin, etoposide, and bleomycin. Examples of growth inhibitory agents include agents that block cell cycle progression (at a place other than S phase), include agents that induce G1 arrest and M-phase arrest. Those agents that arrest G1 also spill over into S-phase arrest, for example, DNA alkylating agents such as tamoxifen, prednisone, dacarbazine, mechlorethamine, cisplatin, methotrexate, 5-fluorouracil, and ara-C. Further information can be found in The Molecular Basis of Cancer, Mendelsohn and Israel, eds., Chapter 1, entitled "Cell cycle regulation, oncogens, and antineoplastic drugs" by Murakami et al. (WB Saunders: Philadelphia, 1995), especially p. 13.

[0149] Examples of such cytokines are lymphokines, monokines, and traditional polypeptide hormones. Included among the cytokines are growth hormone such as human growth hormone, N-methionyl human growth hormone, and bovine growth hormone; parathyroid hormone; thyroxine; insulin; proinsulin; relaxin; prorelaxin; glycoprotein hormones such as follicle stimulating hormone (FSH), thyroid stimulating hormone (TSH), and luteinizing hormone (LH); hepatic growth factor, fibroblast growth factor; prolactin; placental lactogen; tumor necrosis factor-α and -β; mullerian-inhibiting substance; mouse gonadotropin-associated peptide; inhibin; activin; vascular endothelial growth factor; integrin; thrombopoietin (TPO); nerve growth factors such as NGF-β; platelet-growth factor; transforming growth factors (TGFs) such as TGF-α and TGF-β; insulin-like growth factor-I and -II; erythropoietin (EPO); osteoinductive factors; interferons such as interferon-α, -β, and -γ; colony stimulating factors (CSFs) such as macrophage-CSF (M-CSF); granulocyte-macrophage-CSF (GM-CSF); and granulocyte-CSF (G-CSF); interleukins (ILs) such as IL-1, IL-1α, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-11, IL-12; a tumor necrosis factor such as TNF-α or TNF-β; and other polypeptide factors including LIF and kit ligand (KL). As used herein, the term cytokine includes proteins from natural sources or from recombinant cell culture and biologically active equivalents of the native sequence cytokines.

[0150] The invention also pertains to immunoconjugates comprising the binding proteins described herein conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (e.g. an enzymatically active toxin of bacterial, fungal, plant or animal origin, or fragments thereof), or a radioactive isotope (i.e., a radioconjugate).

[0151] Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above. Enzymatically active toxins and fragments thereof which can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolaca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin and the tricothecenes. A variety of radionuclides are available for the production of radioconjugated anti-ErbB2 binding proteins. Examples include 212Bi, 131I, 131In, 90Y and 186Re.

[0152] Immunoconjugates comprising a member of the potent family of antibacterial and antitumor agents, known collectively as the calicheamicins or the LL-E33288 complex, (see U.S. Pat. No. 4,970,198 (1990)) are also contemplated. The most potent of the calicheamicins is designated γ1, which is herein referenced simply as gamma. These compounds contain a methyltrisulfide that can be reacted with appropriate thiols to form disulfides, at the same time introducing a functional group such as a hydrazide or other functional group that is useful in attaching a calicheamicin derivative to a carrier. (See U.S. Pat. No. 5,053,394). Conjugation methods for preparing monomeric calicheamicin derivative/

carrier have been disclosed (see U.S. Pat. No. 5,712,374 and U.S. Pat. No. 5,714,586, incorporated herein in their entirety).

[0153] Conjugates of the binding protein and cytotoxic agent can be made using a variety of bifunctional protein coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutareldehyde), bis-azido compounds (such as bis (p-azidobenzoyl)hexanediamine), bis-diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta et al. Science 238: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the binding protein.

[0154] Effective amounts of the other therapeutic agents are well known to those skilled in the art. However, it is well within the skilled artisan's purview to determine the other therapeutic agent's optimal effective amount range. The binding proteins of the present invention and the other therapeutic agent(s) can act additively or, alternatively, synergistically. In one embodiment of the invention, where another therapeutic agent(s) is administered to an animal, either the effective amount of the binding protein of the present invention or the other therapeutic agent(s) can be administered in an amount that is less than its effective amount would be where the other therapeutic agent is not administered. In this case, without being bound by theory, it is believed that the two (or more) act synergistically.

VI. Diagnostic Uses

[0155] In a further aspect, a binding protein of the invention may also be used to detect the presence of ErbB2 or ErbB2 expressing cells in a biological sample. By correlating the presence or level of ErbB2 with a medical condition, one of skill in the art can diagnose the associated medical condition, including cancer.

[0156] Binding protein-based, including antibody-based detection methods are well known in the art, and include ELISA, radioimmunoassays, immunoblots, Western blots, flow cytometry, immunofluorescence, immunoprecipitation, and other related techniques. The antibodies may be provided in a diagnostic kit that incorporates at least one of these procedures to detect ErbB2. The kit may contain other components, packaging, instructions, or other material to aid the detection of the protein and use of the kit.

[0157] Binding proteins of the invention may be modified with detectable markers, including ligand groups (e.g., biotin), fluorophores and chromophores, radioisotopes, electron-dense reagents, or enzymes. Enzymes are detected by their activity. For example, horseradish peroxidase is detected by its ability to convert tetramethylbenzidine (TMB) to a blue pigment, quantifiable with a spectrophotometer. Other suitable binding partners include biotin and avidin, IgG and protein A, and other receptor-ligand pairs known in the art.

[0158] Binding proteins of the invention can also be functionally linked (e.g., by chemical coupling, genetic fusion, non-covalent association or otherwise) to at least one other molecular entity, such as another antibody (e.g., a bispecific or a multispecific antibody), toxins, radioisotopes, cytotoxic or cytostatic agents, among others for therapeutic use. Other permutations and possibilities are apparent to those of ordinary skill in the art, and they are considered equivalents within the scope of this invention.

[0159] Further, the anti-ERRB2 binding proteins can be used to detect the presence, isolate, and/or to quantitate ErbB2-expressing cells in a sample from a subject or by in vivo imaging.

VII. Pharmaceutical Compositions and Methods of Administration

[0160] In still another aspect, the invention provides compositions comprising an anti-ErbB2 binding protein of the invention. The compositions may be suitable for pharmaceutical use and administration to patients. The compositions comprise a binding protein of the present invention and a pharmaceutically acceptable carrier. The composition may optionally comprise a pharmaceutical excipient. As used herein, "pharmaceutical excipient" includes solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents, etc., that are compatible with pharmaceutical administration. Use of these agents for pharmaceutically active substances is well known in the art. The compositions may also contain other active compounds providing supplemental, additional, or enhanced therapeutic functions. The pharmaceutical compositions may also be included in a container, pack, or dispenser together with instructions for administration.

[0161] A pharmaceutical composition of the invention is formulated to be compatible with its intended route of administration. Methods to accomplish the administration are known to those of ordinary skill in the art. Pharmaceutical compositions may be topically or orally administered, or capable of transmission across mucous membranes. Examples of administration of a pharmaceutical composition include oral ingestion or inhalation. Administration may also be intravenous, intraperitoneal, intramuscular, intracavity, subcutaneous, cutaneous, or transdermal.

[0162] Solutions or suspensions used for intradermal or subcutaneous application typically include at least one of the following components: a sterile diluent such as water, saline solution, fixed oils, polyethylene glycol, glycerine, propylene glycol, or other synthetic solvent; antibacterial agents such as benzyl alcohol or methyl parabens; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid (EDTA); buffers such as acetate, citrate, or phosphate; and tonicity agents such as sodium chloride or dextrose. The pH can be adjusted with acids or bases. Such preparations may be enclosed in ampoules, disposable syringes, or multiple dose vials.

[0163] Solutions or suspensions used for intravenous administration include a carrier such as physiological saline, bacteriostatic water, Cremophor EL™ (BASF, Parsippany, N.J.), ethanol, or polyol. In all cases, the composition must be sterile and fluid for easy syringability. Proper fluidity can often be obtained using lecithin or surfactants. The composition must also be stable under the conditions of manufacture and storage. Prevention of microorganisms can be achieved with antibacterial and antifungal agents, e.g., parabens, chlorobutanol, phenol, ascorbic acid, thimerosal, etc. In many cases, isotonic agents (sugar), polyalcohols (mannitol and sorbitol), or sodium chloride may be included in the composition. Prolonged absorption of the composition can be

accomplished by adding an agent that delays absorption, e.g., aluminum monostearate and gelatin.

[0164] Oral compositions include an inert diluent or edible carrier. The composition can be enclosed in gelatin or compressed into tablets. For the purpose of oral administration, the antibodies can be incorporated with excipients and placed in tablets, troches, or capsules. Pharmaceutically compatible binding agents or adjuvant materials can be included in the composition. The tablets, troches, and capsules, may contain (1) a binder such as microcrystalline cellulose, gum tragacanth or gelatin; (2) an excipient such as starch or lactose, (3) a disintegrating agent such as alginic acid, Primogel, or corn starch; (4) a lubricant such as magnesium stearate; (5) a glidant such as colloidal silicon dioxide; or (6) a sweetening agent or a flavoring agent.

[0165] The composition may also be administered by a transmucosal or transdermal route. For example, antibodies that comprise a Fc portion may be capable of crossing mucous membranes in the intestine, mouth, or lungs (via Fc receptors). Transmucosal administration can be accomplished through the use of lozenges, nasal sprays, inhalers, or suppositories. Transdermal administration can also be accomplished through the use of a composition containing ointments, salves, gels, or creams known in the art. For transmucosal or transdermal administration, penetrants appropriate to the barrier to be permeated are used. For administration by inhalation, the antibodies are delivered in an aerosol spray from a pressured container or dispenser, that contains a propellant (e.g., liquid or gas) or a nebulizer.

[0166] In certain embodiments, the binding proteins of this invention are prepared with carriers to protect against rapid elimination from the body. Biodegradable polymers (e.g., ethylene vinyl acetate, polyanhydrides, polyglycolic acid, collagen, polyorthoesters, polylactic acid) are often used. Methods for the preparation of such formulations are known by those skilled in the art. Liposomal suspensions can be used as pharmaceutically acceptable carriers too. The liposomes can be prepared according to established methods known in the art (U.S. Pat. No. 4,522,811).

[0167] The binding proteins or compositions of the invention are administered in therapeutically effective amounts as described. Therapeutically effective amounts may vary with the subject's age, condition, sex, and severity of medical condition. Appropriate dosage may be determined by a physician based on clinical indications. The binding proteins or compositions may be given as a bolus dose to maximize the circulating levels of protein for the greatest length of time. Continuous infusion may also be used after the bolus dose.

[0168] As used herein, the term "subject" is intended to include human and non-human animals. Subjects may include a human patient having a disorder characterized by cells that express ErbB2, e.g., a cancer cell or an immune cell. The term "non-human animals" of the invention includes all vertebrates, such as non-human primates, sheep, dogs, cows, chickens, amphibians, reptiles, etc.

[0169] Examples of dosage ranges that can be administered to a subject can be chosen from: 1 μg/kg to 20 mg/kg, 1 μg/kg to 10 mg/kg, 1 μg/kg to 1 mg/kg, 10 μg/kg to 1 mg/kg, 10 μg/kg to 100 μg/kg, 100 μg/kg to 1 mg/kg, 250 μg/kg to 2 mg/kg, 250 μg/kg to 1 mg/kg, 500 μg/kg to 2 mg/kg, 500 μg/kg to 1 mg/kg, 1 mg/kg to 2 mg/kg, 1 mg/kg to 5 mg/kg, 5 mg/kg to 10 mg/kg, 10 mg/kg to 20 mg/kg, 15 mg/kg to 20 mg/kg, 10 mg/kg to 25 mg/kg, 15 mg/kg to 25 mg/kg, 20 mg/kg to 25 mg/kg, and 20 mg/kg to 30 mg/kg (or higher). These dosages may be administered daily, weekly, biweekly, monthly, or less frequently, for example, biannually, depending on dosage, method of administration, disorder or symptom(s) to be treated, and individual subject characteristics. Dosages can also be administered via continuous infusion (such as through a pump). The administered dose may also depend on the route of administration. For example, subcutaneous administration may require a higher dosage than intravenous administration.

[0170] In certain circumstances it may be advantageous to formulate compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited for the patient. Each dosage unit contains a predetermined quantity of antibody calculated to produce a therapeutic effect in association with the carrier. The dosage unit depends on the characteristics of the antibodies and the particular therapeutic effect to be achieved.

[0171] Toxicity and therapeutic efficacy of the composition can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., determining the LD_{50} (the dose lethal to 50% of the population) and the ED_{50} (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD_{50}/ED_{50}. Binding proteins that exhibit large therapeutic indices may be less toxic and/or more therapeutically effective.

[0172] The data obtained from the cell culture assays and animal studies can be used to formulate a dosage range in humans. The dosage of these compounds may lie within the range of circulating antibody concentrations in the blood, that includes an ED_{50} with little or no toxicity. The dosage may vary within this range depending upon the dosage composition form employed and the route of administration. For any antibody used in the present invention, the therapeutically effective dose can be estimated initially using cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the IC_{50} (i.e., the concentration of antibody that achieves a half-maximal inhibition of symptoms). The effects of any particular dosage can be monitored by a suitable bioassay. Examples of suitable bioassays include DNA replication assays, transcription-based assays and ErbB2 binding assays.

EXAMPLES

Example 1

Selection of Anti-ErbB2 scFv's

[0173] Single chain fragment variable (scFv) moieties that bind to the extracellular domain (ECD) of Her2 (ErbB2) were identified following three rounds of selection using three phagemid libraries: the Bone Marrow Vaughan (BMV) library (Vaughan et al, 1996), the combined spleen (CS) library and the DP47 library (unpublished). Several Her2-Fc proteins or cell lines expressing various forms of Her2 were used during the selection and subsequent screening steps (see Table 3). The selection strategies are outlined in FIG. **1**.

[0174] Selection Using Biotinylated HER2 Proteins

[0175] For selections involving biotinylated protein, aliquots of phage and magnetic streptavidin beads (Dynabeads M-280 streptavidin) were blocked separately in 3% milk/PBS for 1 hour at room temperature in a rotary mixer (20 rpm). Each selection was preceded by a de-selection step. For de-

selection, blocked phage were incubated with the pre-blocked magnetic beads and incubated for one hour on a rotary shaker (20 rpm). The de-selected library was collected by pelleting the beads using a magnetic separator. A 1 μM concentration of a non-biotinylated competitor protein (eg, irrelevant MIgG2a protein) was added to the de-selected phage and incubated for a further hour.

[0176] Biotinylated selection antigen (at various concentrations as indicated in FIG. **1**) was incubated with the de-selected phage library for 2 hours at room temp on a rotary mixer (20 rpm) followed by a 15 minute incubation with pre-blocked magnetic beads. Beads were separated using a magnetic separator and washed 10 times with PBS/0.1% Tween 20 and 3 times with PBS. Bound phage were eluted by incubation with a 10 ug/ml solution of trypsin in PBS for 30 minutes at 37° C. (100 rpm) followed by separation from the magnetic beads.

[0177] Selection Using Cells Expressing HER2ECD or ECD Fragments

[0178] For selections involving cells, approximately 4×10^7 de-selection cells (ie. cells not expressing the antigen of interest) and 2×10^7 capture (i.e., selection) cells (cells expressing the antigen of interest) were collected using PBS/5 mM EDTA and washed twice with PBS. Cells were blocked with 3% milk/1% BSA/PBS for 1 hour at 4° C. on a rotary mixer (20 rpm). De-selection cells were collected by centrifugation, re-suspended in blocked phage and incubated at 4° C. as before. Both the capture and de-selection cells were pelleted and the capture cells were resuspended with the de-selected phage supernatant and incubated at 4° C. as before. The capture cells were washed three times with cold PBS/0.1% Tween 20 and three times with cold PBS. Phage were eluted by re-suspending the cells in a 10 μg/ml trypsin solution and incubated for 30 min at 37° C. (100 rpm). Eluted phage were harvested in the supernatant following centrifugation of cells. Eluted phage were used to infect 10 ml of an *E. coli*TG1 culture that had been grown to mid-logarithmic phase (corresponding to an OD_{600} of ~0.5). Bacteria were infected with phage for 1 hour at 37° C. with shaking at 150 rpm, concentrated following a centrifugation step and plated on 2×TY agar bioassay plates containing 2% glucose and 100 ug/ml ampicillin (2×TYAG). Various dilutions of *E. coli* culture infected with either input or output phage were also plated on 2×TYAG agar to determine phage titers. Following overnight growth at 30° C., 10 ml of 2×TYAG medium was added to each bioassay plate and the cells were re-suspended by scraping the bacterial lawn. Glycerol was added to this cell suspension to give a final concentration of 17% and stored in aliquots at −80° C. until further use. To rescue phage for the next round of selection, 100 μl of this cell suspension was used to inoculate 20 ml 2×TYAG medium, that was grown at 37° C. (300 rpm) to an OD_{600} of 0.3-0.5. Cells were then super-infected with 3.3 μl of MK13K07 helper phage and incubated at 37° C. (150 rpm) for 1 hour. The cells were then centrifuged and the pellet re-suspended in a kanamycin/non-glucose containing medium (2×TY with 50 μg/ml kanamycin and 100 ug/ml ampicillin). This culture was grown overnight at 30° C. (300 rpm). Phage were harvested in the supernatant following centrifugation and were ready to use in the second and third rounds of selection as described in FIG. **1**.

TABLE 3

Name	Description	Sequence for Her2 region of fusion protein
Her008P (Synonyms: ECD; SIIS; HER008)	Full-length extracellular domain (ECD) of Her2 expressed with a mIgG2a Fc tail	MELAALCRWGLLLALLPPGAASTQV CTGTDMKLRLPASPETHLDMLRHLY QGCQVVQGNLELTYLPTNASLSFLQ DIQEVQGYVLIAHNQVRQVPLQRLR IVRGTQLFEDNYALAVLDNGDPLNN TTPVTGASPGGLRELQLRSLTEILK GGVLIQRNPQLCYQDTILWKDIFHK NNQLALTLIDTNRSRACHPCSPMCK GSRCWGESSEDCQSLTRTVCAGG CARCKGPLPTDCCHEQCAAGCTGP KHSDCLACLHFNHSGICELHCPALV TYNTDTFESMPNPEGRYTFGASCV TACPYNYLSTDVGSCTLVCPLHNQE VTAEDGTQRCEKCSKPCARVCYGL GMEHLREVRAVTSANIQEFAGCKKI FGSLAFLPESFDGDPASNTAPLQPE QLQVFETLEEITGYLYISAWPDSLPD LSVFQNLQVIRGRILHNGAYSLTLQ GLGISWLGLRSLRELGSGLALIHHN THLCFVHTVPWDQLFRNPHQALLH TANRPEDECVGEGLACHQLCARGH CWGPGPTQCVNCSQFLRGQECVE ECRVLQGLPREYVNARHCLPCHPE CQPQNGSVTCFGPEADQCVACAH YKDPPFCVARCPSGVKPDLSYMPI WKFPDEEGACQPCPINCTHSCVDL DDKGCPAEQRASPLTSIIS (SEQ ID NO: 242)

TABLE 3-continued

Name	Description	Sequence for Her2 region of fusion protein
Her017P (Synonyms: EQR; HER017)	Her2 ECD with a deletion in the membrane proximal 9 amino acids expressed with a mIgG2a Fc tail	MELAALCRWGLLLALLPPGAASTQV CTGTDMKLRLPASPETHLDMLRHLY QGCQVVQGNLELTYLPTNASLSFLQ DIQEVQGYVLIAHNQVRQVPLQRLR IVRGTQLFEDNYALAVLDNGDPLNN TTPVTGASPGGLRELQLRSLTEILK GGVLIQRNPQLCYQDTILWKDIFHK NNQLALTLIDTNRSRACHPCSPMCK GSRCWGESSEDCQSLTRTVCAGG CARCKGPLPTDCCHEQCAAGCTGP KHSDCLACLHFNHSGICELHCPALV TYNTDTFESMPNPEGRYTFGASCV TACPYNYLSTDVGSCTLVCPLHNQE VTAEDGTQRCEKCSKPCARVCYGL GMEHLREVRAVTSANIQEFAGCKKI FGSLAFLPESFDGDPASNTAPLQPE QLQVFETLEEITGYLYISAWPDSLPD LSVFQNLQVIRGRILHNGAYSLTLQ GLGISWLGLRSLRELGSGLALIHHN THLCFVHTVPWDQLFRNPHQALLH TANRPEDECVGEGLACHQLCARGH CWGPGPTQCVNCSQFLRGQECVE ECRVLQGLPREYVNARHCLPCHPE CQPQNGSVTCFGPEADQCVACAH YKDPPFCVARCPSGVKPDLSYMPI WKFPDEEGACQPCPINCTHSCVDL DDKGCPAEQR (SEQ ID NO: 243)
Her018P (Synonyms: 1.8; HER018)	Her2 ECD with a deletion in the CR2 (Domain IV) region expressed with a mIgG2a Fc tail	MELAALCRWGLLLALLPPGAASTQV CTGTDMKLRLPASPETHLDMLRHLY QGCQVVQGNLELTYLPTNASLSFLQ DIQEVQGYVLIAHNQVRQVPLQRLR IVRGTQLFEDNYALAVLDNGDPLNN TTPVTGASPGGLRELQLRSLTEILK GGVLIQRNPQLCYQDTILWKDIFHK NNQLALTLIDTNRSRACHPCSPMCK GSRCWGESSEDCQSLTRTVCAGG CARCKGPLPTDCCHEQCAAGCTGP KHSDCLACLHFNHSGICELHCPALV TYNTDTFESMPNPEGRYTFGASCV TACPYNYLSTDVGSCTLVCPLHNQE VTAEDGTQRCEKCSKPCARVCYGL GMEHLREVRAVTSANIQEFAGCKKI FGSLAFLPESFDGDPASNTAPLQPE QLQVFETLEEITGYLYISAWPDSLPD LSVFQNLQVIRGRILHNGAYSLTLQ GLGISWLGLRSLRELGSGLALIHHN THLCFVHTVPWDQLFRNPHQALLH TANRPEDECVGEGLACHQLCARGH CWGPGPTQCVNCSQFLRGQECVE ECRVLQGLPREYVNARHCLPCHPE CQPQNGSVTCFGPEADQCVACAH YKDPPFCVAR (SEQ ID NO: 244)
Her054P (Synonyms: L1-CR1; 1.0)	Domains I (L1) and II (CR-1) of Her2 expressed with a mIgG2a Fc tail	MELAALCRWGLLLALLPPGAASTQV CTGTDMKLRLPASPETHLDMLRHLY QGCQVVQGNLELTYLPTNASLSFLQ DIQEVQGYVLIAHNQVRQVPLQRLR IVRGTQLFEDNYALAVLDNGDPLNN TTPVTGASPGGLRELQLRSLTEILK GGVLIQRNPQLCYQDTILWKDIFHK NNQLALTLIDTNRSRACHPCSPMCK GSRCWGESSEDCQSLTRTVCAGG CARCKGPLPTDCCHEQCAAGCTGP KHSDCLACLHFNHSGICELHCPALV TYNTDTFESMPNPEGRYTFGASCV TACPYNYLSTDVGSCTLVCPLHNQE VTAEDGTQRCEKCSKPC (SEQ ID NO: 245)

TABLE 3-continued

Name	Description	Sequence for Her2 region of fusion protein
Full length HER2		MELAALCRWGLLLALLPPGAASTQV CTGTDMKLRLPASPETHLDMLRHLY QGCQVVQGNLELTYLPTNASLSFLQ DIQEVQGYVLIAHNQVRQVPLQRLR IVRGTQLFEDNYALAVLDNGDPLNN TTPVTGASPGGLRELQLRSLTEILK GGVLIQRNPQLCYQDTILWKDIFHK NNQLALTLIDTNRSRACHPCSPMCK GSRCWGESSEDCQSLTRTVCAGG CARCKGPLPTDCCHEQCAAGCTGP KHSDCLACLHFNHSGICELHCPALV TYNTDTFESMPNPEGRYTFGASCV TACPYNYLSTDVGSCTLVCPLHNQE VTAEDGTQRCEKCSKPCARVCYGL GMEHLREVRAVTSANIQEFAGCKKI FGSLAFLPESFDGDPASNTAPLQPE QLQVFETLEEITGYLYISAWPDSLPD LSVFQNLQVIRGRILHNGAYSLTLQ GLGISWLGLRSLRELGSGLALIHHN THLCFVHTVPWDQLFRNPHQALLH TANRPEDECVGEGLACHQLCARGH CWGPGPTQCVNCSQFLRGQECVE ECRVLQGLPREYVNARHCLPCHPE CQPQNGSVTCFGPEADQCVACAH YKDPPFCVARCPSGVKPDLSYMPI WKFPDEEGACQPCPINCTHSCVDL DDKGCPAEQRASPLTSIISAVVGILL VVVLGVVFGILIKRRQQKIRKYTMRR LLQETELVEPLTPSGAMPNQAQMRI LKETELRKVKVLGSGAFGTVYKGIW IPDGENVKIPVAIKVLRENTSPKANK EILDEAYVMAGVGSPYVSRLLGICLT STVQLVTQLMPYGCLLDHVRENRG RLGSQDLLNWCMQIAKGMSYLEDV RLVHRDLAARNVLVKSPNHVKITDF GLARLLDIDETEYHADGGKVPIKWM ALESILRRRFTHQSDVWSYGVTVW ELMTFGAKPYDGIPAREIPDLLEKGE RLPQPPICTIDVYMIMVKCWMIDSE CRPRFRELVSEFSRMARDPQRFVVI QNEDLGPASPLDSTFYRSLLEDDD MGDLVDAEEYLVPQQGFFCPDPAP GAGGMVHHRHRSSSTRSGGGDLT LGLEPSEEEAPRSPLAPSEGAGSDV FDGDLGMGAAKGLQSLPTHDPSPL QRYSEDPTVPLPSETDGYVAPLTCS PQPEYVNQPDVRPQPPSPREGPLP AARPAGATLERPKTLSPGKNGVVK DVFAFGGAVENPEYLTPQGGAAPQ PHPPPAFSPAFDNLYYWDQDPPER GAPPSTFKGTPTAENPEYLGLDVPV (SEQ ID NO: 246)

Example 2

Preparation of Phage or Crude Periplasmic Material for Use in ELISAs

[0179] ScFvs can be expressed either on the surface of a phage particle or in solution in the bacterial periplasmic space, depending upon the growth conditions used. To induce release of scFv into the periplasm, 96-deepwell plates containing 2×TY media with 0.1% glucose/100 μg/ml ampicillin were inoculated from thawed glycerol stocks (one clone per well) using the QPix2 Colony picker (Genetix) and grown at 37° C. (999 rpm) for ~4 hours. Cultures were induced with IPTG at a final concentration of 0.02 mM and grown overnight at 30° C. (999 rpm). The contents of the bacterial periplasm (peripreps) were released by osmotic shock. Briefly, plates were centrifuged and pellets were resuspended in 150 μl HEPES periplasmic buffer (50 mM HEPES, pH7.4/0.5 mM EDTA/20% Sucrose), followed by the addition of 150 μl 1:5 HEPES:water and incubated on ice for 30 minutes. Plates were centrifuged and the scFv-containing supernatant was harvested.

[0180] To prepare phage expressing scFv on their surface, 96-well plates containing 150 μl 2×TY media with 2% glucose/100 μg/ml ampicillin were inoculated from thawed glycerol stocks as described above and grown at 37° C. (700 rpm) for ~4 hours. 20 μl of a 1:1000 dilution of helper phage (~2×10^8 pfu) was added and the plates incubated for a further hour at 37° C. (300 rpm). Plates were centrifuged and the media was replaced with a kanamycin/non-glucose containing media (2×TY with 50 μg/ml kanamycin and 100 ug/ml

ampicillin). Plates were grown overnight at 30° C. (700 rpm) and phage were harvested in the supernatant following centrifugation.

[0181] Thirty-one Her2-binding ScFv's were identified by three rounds of screenings as illustrated in FIG. **1**. These ScFv's specifically bind to the ECD region of Her2.

[0182] Among these thirty-one Her2-binding ScFv's, fourteen ScFv's were expressed on the surface of a phage particle for the purpose of screening. These ScFv's are: S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_1E1, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_1A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, and S1R3C1_CS_1B10 (FIGS. **2** and **3**).

[0183] The remaining seventeen ScFv's were expressed in bacterial periplasm in soluble form for the purpose of screening: S1R3A1_BMV_1F3, S1R3B1_BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11, S1R3B1_BMV_1A10, S1R3A1_CS_1D11, S1R3C1_DP47_1H1, S1R3A1_CS_1B12, S1R3B1_BMV_1H5, S1R3A1_DP47_1A6, S1R3B1_DP47_1E1, and S1R3B1_BMV_1A1 (FIGS. **2** and **3**).

Example 3

ELISA to Test Her2 Protein Construct Binding by scFvs Expressed in the *E. coli* Periplasm, on the Surface of Phage, or in Mammalian Cells as Fc Fusions

[0184] Various Her2-Fc proteins (e.g., Her008P, Her017P, Her018P, etc.) or a negative control murine IgG2a protein were coated overnight at 4° C. on 96-well Nunc Maxisorp at a concentration of 1 ug/ml in PBS. Alternatively, pre-blocked streptavidin-coated plates (Greiner) were coated with biotinylated Her2-Fc proteins for 1 hour at room temperature at a concentration of 1 ug/ml in block buffer (3% skim milk/1% BSA/PBS). Plates were washed three times using PBS and blocked for 1 hour at room temperature in 3% skim milk/1% BSA/PBS. Phage or peripreps were prepared as described above and were blocked for 1 hour at room temperature in an equal volume of 6% skim milk/1% BSA/PBS. Blocked plates were washed five times with PBS and 50 μl/well of blocked phage or periprep were transferred to the appropriate plates and incubated for 1 hour at room temperature. A 1 ug/ml solution of HERCEPTIN® (trastuzumab) (in blocking buffer) was added to well H12 of each plate to serve as a positive control. Plates were washed five times with PBS prior to the addition of a 1:250 dilution of anti-myc peroxidase (Roche), a 1:2500 dilution of anti-M13 peroxidase (Amersham Biosciences) or a 1:5000 or 1:1000 dilution of goat anti-human peroxidase (Southern Biotech) secondary antibody to detect bound scFv, phage, HERCEPTIN® (trastuzumab) or SMIP, respectively. Plates were incubated for a further hour at room temperature and washed seven times with PBS. Signal was developed using TMB, the reaction stopped with H_2SO_4 and the absorbance read at 450 nm on an Envision plate reader (Perkin Elmer). The results of these binding assays are shown in FIG. **5**.

[0185] Alternatively, plates were coated with 1 ug/ml of a SMIP (Her030, Her033/Her067, Her018) or antibody (Herceptin®), positive control). SMIPs were used to capture 3-fold serial dilution (9-0 μg/ml) of soluble protein sample as follows: dimeric HER2 (HERB017), monomeric HER2 (HER155), or monomeric HER2 (shed ectodomain from SKBR3 supernatant). Captured soluble protein was detected using 0.1 mg/ml anti-c-Erb B2/c-Neu (Ab-5) mouse mAb (TA-1; binds ECD; Calbiochem) and detected using HRP-conjugated Goat anti-mouse IgG (Fcg Subclass 1 specific; Jackson ImmuonoResearch).

[0186] The results of the SMIP binding assays are shown in FIG. **6**A-C, FIG. **7**A-**7**D and FIG. **8**. In FIG. **8**, the binding of HER018, HER026-HER039 and Herceptin® (trastuzumab) to Her2 protein constructs was scored as –, +, ++ or +++, while the binding of HER071-HER087 to Her2 protein constructs was scored as a – or +.

Example 4

ELISA to Measure Binding of scFvs (Expressed in the Periplasm or on the Surface of Phage) to Her2-Expressed Cells

[0187] 2×10^4 CHOK1 cells/well were seeded in a 96-well tissue culture plate on Day 1 and incubated at 37° C./5% CO_2 for 2-4 days until a confluent monolayer was observed. Cells were washed five times with PBS (+ Ca/Mg ions) and blocked for 1 hour at room temperature with 3% skim milk/1% BSA/PBS (+ Ca/Mg ions). Phage or peripreps were prepared as described above and were blocked for 1 hour at room temperature in an equal volume of 6% skim milk/1% BSA/PBS (+ Ca/Mg ions). Blocked plates were washed five times with PBS (+ Ca/Mg ions) and 50 μl/well of blocked phage or periprep were transferred to the appropriate plates and incubated for 1 hour at room temperature. A 1 ug/ml solution of HERCEPTIN® (trastuzumab) (in blocking buffer) was added to well H12 of each plate to serve as a positive control. Plates were washed five times with PBS (+Ca/Mg ions) prior to the addition of a 1:250 dilution of anti-myc peroxidase (Roche), a 1:2500 dilution of anti-M13 peroxidase (Amersham Biosciences) or a 1:5000 dilution of goat anti-human (Southern Biotech) secondary antibody to detect bound scFv, phage or HERCEPTIN® (trastuzumab) respectively. Plates were incubated for a further hour at room temperature and washed ten times with PBS (+ Ca/Mg ions). Signal was developed using TMB, the reaction stopped with H_2SO_4 and the absorbance read at 450 nm on an ENVISION plate reader (Perkin Elmer). The results of these binding assays are shown in FIG. **5**.

[0188] Alternatively, the cell lines tested for SMIP binding included SKBR3, BT474, 22rv1, MDA-MB-175, MDA-MB-453, MDA-MB-361 (ATCC), MDA-MB-361 (JL), and Ramos ($Her2^-/CD20^+$ control). The SMIPs tested included Her067 (c.f. Her033), Her094 (c.f. Her030), and Her018, while the controls used included Herceptin® (trastuzumab), Rituxan® (anti-CD20 mAb rituximab), and CD20-SMIP.

[0189] Each well of a 6 well plate was seeded with 2×10^5 cells and incubated overnight at 37° C./5% CO_2. Cells were then treated with antibody or SMIP (at 10 ug/ml final) (in triplicate) and incubated for another 24 or 48 hours. After incubation, the cells were pulsed with 50 uM BrdU (Sigma) for 30 minutes at 37° C., the media was removed, and the cells were treated with trypsin (except Ramos) and then $3\text{-}3.5\times10^5$ cells per well were stained in 100 μl Staining Buffer in the presence or absence of a SMIP or antibody one of three different concentrations (ranging from 200 nM to 0.27 nM). The SMIP or antibody treatment was removed and the cells were washed three times with PBS, pH 7.2-7.4 with 0.1% TWEEN®-20 (PBS-T). A secondary antibody (5 ug/ml Alexa

Fluor 488-conjugated Goat anti-Human IgG; Molecular Probes) was then added and incubated for 1-2 hours at room temperature. The secondary antibody was removed and the cells washed again three times with PBS-T. The cells were then fixed in 1% paraformaldehyde in Staining Buffer and analyzed 1 hour to 1 day later.

[0190] SMIPs maintain a similar staining pattern regardless of the amount of HER2 on the cell surface and the other ErbB receptors/ligands expressed by the cell lines (relative surface staining for ErbB1, Her2, Erb3 and production of ligand by cell lines is not shown). The SMIP/antibody staining pattern was Herceptin®>Her018>HER067 (Her033)>HER094 (Her030). The results of these binding assays are shown in FIG. **8** and FIG. **9**A-**9**H. (In FIG. **9**E, 0.82 nM HER094 data not collected due to mechanical error.)

Example 5

PCR Amplification of scFv Regions for Sequencing Analysis

[0191] PCR amplification of scFvs was carried out using the KOD HOT START DNA Polymerase kit (Novagen) in accordance with the manufacturers instructions. 0.2 μM each of the M13rev (5' GGAAACAGCTATGACCATGA 3') (SEQ ID NO: 247) forward and Mycseq (5' CTCTTCTGAGATGAGTTTTTG 3') (SEQ ID NO: 248) reverse primers were used. 5 μl of a 1:10 dilution of a stationary phase bacterial culture was used as the template for a final reaction volume of 20 μl. The cycling conditions used were a 2 minute hot start at 94° C., 25 cycles of denaturation at 94° C. (1 minute), primer annealing at 42° C. (30 seconds) and extension at 72° C. (1 min), followed by a final 5 minute extension at 72° C. PCR products were verified by agarose gel electrophoresis and cleaned up with ExoI/SAP (shrimp alkaline phosphatase) prior to sequencing of both strands with primers 145837 (5' GGAGATTTTCAACGTGAA 3') (SEQ ID NO: 249) and 142051 (5' CTCTTCTGAGATGAGTTTTTG 3') (SEQ ID NO: 250). The closest human germlines of the V_H and V_L segments were determined (Table 4).

TABLE 4

V_H and V_L germlines of ERBB2 clones

Mab	Human V_H germline gene	Human V_L germline gene
S1R2A_CS_1F7	1-02 (DP8/75)	Vλ 3h
S1R2A_CS_1D11	1-69 (DP10)	Vλ 1b (DPL5)
S1R2C_CS_1D3	1-69 (DP10)	Vλ 1b (DPL5)
S1R2C_CS_1H12	3-48 (DP51)	Vλ 1c (DPL2)
S1R2A_CS_1D3	1-02 (DP8/75)	Vλ 1g (DPL3)
S1R3B2_BMV_1E1	3-33 (DP50)	Vλ 1b (DPL5)
S1R3C1_CS_1D3	6-1 (DP74)	Vλ 2c
S1R3B2_DP47_1E8	3-23 (DP47)	Vλ 1e (DPL8)
S1R3B2_BMV_1G2	1-18 (DP14)	Vκ L12
S1R3B2_BMV_1H5	3-33 (DP50)	Vλ 2a2 (DPL11)
S1R3C1_CS_1A6	5-51 (DP73)	Vλ 1c (DPL2)

TABLE 4-continued

V_H and V_L germlines of ERBB2 clones

Mab	Human V_H germline gene	Human V_L germline gene
S1R3B2_DP47_1C9	3-23 (DP47)	Vλ 1c (DPL2)
S1R3B2_DP47_1E10	3-23 (DP47)	Vλ 1g (DPL3)
S1R3C1_CS_1B10	1-69 (DP10)	Vλ 6a
S1R3A1_BMV_1F3	3-21 (DP77)	Vλ 3l (DPL16)
S1R3B1_BMV_1G11	3-23 (DP47)	Vλ 2a2 (DPL11)
S1R3A1_BMV_1G4	1-03 (DP25)	Vλ 2a2 (DPL11)
S1R3B1_BMV_1H11	3-23 (DP47)	Vκ L12
S1R3A1_CS_1B9	5-51 (DP73)	Vλ 8a (DPL21)
S1R3B1_BMV_1H9	4-04 (DP70)	Vλ 3l (DPL16)
S1R3A1_CS_1B10	1-02 (DP8/75)	Vλ 8a (DPL21)
S1R3B1_BMV_1C12	3-30.5 (DP49)	Vλ 1c (DPL2)
S1R3C1_BMV_1H11	3-33 (DP50)	Vλ 1e (DPL8)
S1R3B1_BMV_1A10	3-30.5 (DP49)	Vλ 3l (DPL16)
S1R3A1_CS_1D11	5-51 (DP73)	Vλ 8a (DPL21)
S1R3C1_DP47_1H1	3-23 (DP47)	Vλ 3h
S1R3A1_CS_1B12	1-02 (DP8/75)	Vλ 1e (DPL8)
S1R3B1_BMV_1H5	3-33 (DP50)	Vλ 3l (DPL16)
S1R3A1_DP47_1A6	3-23 (DP47)	Vλ 1c (DPL2)
S1R3B1_DP47_1E1	3-23 (DP47)	Vλ 6a
S1R3B1_BMV_1A1	1-18 (DP14)	Vλ 2a2 (DPL11)

Example 6

BIACORE® Binding Assay

[0192] Binding of different Her2-directed binders (antibodies and SMIPs) to monomeric Her2 ECD and truncations of dimeric Her2 ECD were determined using a BIACORE® T100 instrument (GE Healthcare, Biacore, Piscataway, N.J.). Her2-directed binders were captured by a monoclonal mouse anti-human Fc (GE healthcare), which was covalently conjugated to a carboxylmethyl dextran surface (CM4) via amines using N-ethyl-N'-(3-dimethylaminopropyl)-carbodiimide hydrochloride and N-hydroxysuccinimide. The unoccupied sites of the activated surface were blocked by ethanolamine. The capturing antibody (referred to as anti hFc) binds to the C_H2 domain of IgG Fc of all sub-classes and showed no discernible dissociation from the captured her2-binders during the course of the assay. Every cycle, 3 different Her2 binders and a non-binder (negative control) were individually captured by anti hFc on 4 different flow cells, typically to about 50 RU, followed by injection of the analyte (Her2 dimers and monomer) at a particular concentration for 10 minutes over all flow cells. The dissociation of the formed complexes were subsequently followed for 12 minutes. At the

end of the cycle, the surface was regenerated gently using 3M $MgCl_2$ which dissociates protein bound to the capturing anti hFc antibody. Multiple such cycles were performed to study binding of different analytes at different concentrations, in the range of 0-300 nM, for each set of three Her2 binders captured. Her2 binders were reproducibly captured every cycle with CV not exceeding 1%. The binding was performed at 25° C. in 0.01 M HEPES pH 7.4, 0.15 M NaCl, 0.005% v/v SURFACTANT P20. Signal associated with binding to the negative control was used to subtract for bulk refractive changes. The kinetic parameters and affinities were determined using BIAEVALUATION software.

[0193] HERCEPTIN® (trastuzumab) bound monomeric EQR, dimeric ECD and shed ECD (monomeric), weakly bound HER018 but did not bind a truncated fusion protein lacking the CR2 domain. In contrast, HER033 and HER030 bound only dimeric ECD and dimeric HER018 but did not bind monomeric EQR or shed ectodomain (ECD). Specifically for dimeric HER2 may be advantageous in that such binders may have increased selectivity for tumors and may not bind, or show reduced binding to tissues that express low levels of HER2 and/or where ligand independent homodimer formation is limited. Such HER2 binders with reduced binding to non-tumor target tissues (e.g., cardiac tissues) may, thus, have fewer side effects including lower toxicity. In addition, a lack of binding to shed HER2 ectodomain would reduce the effective dose compared to a HER2-binding agent that has significant binding to shed ECD.

[0194] The results of the BIACORE® assay are shown in FIG. **7**.

[0195] Trastuzumab and the SMIP version of trastuzumab (HER018) bind full length dimer and monomer soluble receptors similarly at low nanomolar levels (about 1 to about 5 nM), whereas truncated dimer soluble receptors (i.e., lacking all three trastuzumab contact sites) are bound poorly or not at all (see Table 5). In contrast, Her030 and Her033/Her067 SMIPs bind soluble dimer receptors at nanomolar affinities (about 4 to about 8 nM), but not monomer HER2. The HER033 and HER067SMIPs have the same amino acid sequence, but the difference between them is that the former is produced in HEK cells while the latter is produced in CHO cells. Binding by HER033 and HER067SMIPs is substantially the same. HER030 appears to bind less strongly than Her033/Her067 to the dimers.

TABLE 5

BIACORE ® binding affinity summary

	Affinity (nM) at 25° C.				
	Herceptin	Her 018	Her 033	Her 067	Her 030
SIIS (Dimer)	1.06	1.4	7.23	8.18	35.6
1.8 (Dimer)	228	167	4.92	6.47	27.6
1.6 (Dimer)	NB	NB	NB	NB	NB
SIIS (Monomer) (Her155)	3.44	4.59	508	ND	ND

NB—No Binding Observed
ND—not enough binding to fit

Example 7

BrdU and ATP Proliferation Assays

[0196] To 96-well plates, cells were added at 2.5×10^3 cells/well (SKBR3, BT474, MDA-MB-453, MDA-MB-175) or at 5×10^3 cells/well (MDA-MB-361). The next day, SMIPs were added to the cells at the desired concentration and then incubated at 37° C./5% CO_2 for 4 (SKBR3, MDA-MB-453, MDA-MB-361, MDA-MB-175), 5 (BT474), or 7 (MDA-MB-361) days. The day before cells were harvested, 5-bromo-2'-deoxyuridine (BrdU) is added to a final concentration of 0.1 mM and continued to incubate overnight at 37° C. After incubation, media was removed and then the cells were treated with ethanol-based fix solution (DELFIA® Cell Proliferation Kit, Perkin Elmer, Waltham, Mass.) at room temperature (RT) for 30 minutes. Fix solution was removed by aspiration, 100 μl/well anti-BrdU-Eu labeled antibody (0.5 mg/mL) was added, and the cells were incubated at RT for 2 hours. Cells were then washed 4 times with Tris-based DELFIA Platewash (300 μl/well/wash). DELFIA Inducer (with Triton) X-100, glycine, HCl, and chelator) was then added to the cells (200 μl/well) and incubated with shaking for 15 minutes at RT. Fluorescence was measured using Flex Station) 3 in Time resolved fluorescence mode (Molecular Devices, Sunnyvale, Calif.).

[0197] After the proliferation assay fluorescence reading, the DELFIA Inducer was removed by aspiration and Hoechst 33342 nuclear stain solution (Invitrogen, Carlsbad, Calif.) was added to the cells. Nuclear stain fluorescence was measured on an IN Cell Analyzer at 4× resolution.

[0198] Alternatively, we investigated anti-Her2 SMIP antiproliferation activity in MDA-MB-361 cells as follows. MDA-MB-361 breast cancer cells were plated in 96-well format and treated with anti-Her2 or control reagents for indicated concentrations and times (24-96 hr). For proliferation assays, media (DMEM plus 10% FBS) was removed, the cells washed with phosphate-buffered saline (PBS), fixed with 4% paraformaldehyde and nuclei stained with DAPI (Molecular Probes). Stained nuclei were counted using Cellomics High Content assay measuring fluorescence at 360 nM. For apoptosis assay, fixed cells were permeabilized by treatment with 0.2% Triton 100 in PBS prior to primary staining with mouse anti-cleaved PARP antibody (Cell Signaling Technologies) and secondary staining with goat anti-mouse IgG labeled with ALEXA488 (Invitrogen). Fluorescence was measured in Cellomics High Content assay at 488 nM.

[0199] ATP Lite First Step assay (Perkin Elmer) was used to assess cellular viability by measuring ATP levels via luminescence (ATP luciferase). To 96-well plates, cells were added at 2.5×10^3 cells/well (SKBR3, BT474, MDA-MB-453, MDA-MB-175) or at 5×10^3 cells/well (MDA-MB-361). The next day, SMIPs were added to the cells at the desired concentration and then incubated at 37° C./5% CO_2 for 4 (SKBR3, MDA-MB-453, MDA-MB-361, MDA-MB-175), 5 (BT474), or 7 (MDA-MB-361) days. After SMIP incubation for the desired amount of time, lyophilized ATP Lite substrate is reconstituted with 10 ml of ATP Lite substrate/lysis solution and allowed to sit at room temperature for 10 minutes. This reconstituted substrate solution was added to the cells (100 μl/well) and read luminescence on Top Count Reader (Packard).

[0200] The results of the proliferation assays are shown in FIGS. **10-12**.

Example 8

Pathway Phosphorylation Assays

[0201] To 96-well plates, cells were added at $8\text{-}12\times10^3$ cells/well depending on cell type (Becton-Dickinson, San

Jose, Calif.) and allowed to incubate overnight in growth medium with serum at 37° C./5% CO_2. After removal of growth medium, the cells were washed with serum-free medium, aspirated, and then serum-free media was added for incubation at 37° C./5% CO_2 for 3 hours. The SMIP of interest was prepared in prewarmed serum-free media, added to each well at the indicated concentration, and incubated at 37° C./5% CO_2 for desired time points. As a control, signaling was inhibited with AG825 (Calbiochem, LaJolla, Calif.) at 40 μM; LY294002 (Cell Signaling) at 50 μM; or U0126 MEK1/2 inhibitor (Cell Signaling) at 10 μM. The cells were then fixed in formaldehyde (diluted in 1×PBS) at a final concentration of 3.7% for 10 minutes at 37° C./5% CO_2. The cells were then washed two times with PBS. After removing the PBS, the cells were permeabilized in 0.1% Triton® X-100 (Sigma-Aldrich, St. Louis, Mo.) solution diluted in 1×PBS at room temperature for 5 minutes. The cells were then washed two times with PBS and blocked by incubation in PBS/1% BSA (Sigma-Aldrich) at room temperature for 30 minutes (or overnight at 4° C.).

[0202] The blocking solution was removed and primary antibody (in PBS with 3% horse serum or PBS with 1% BSA, and 0.1% Triton® X-100) was added for 1 hour at room temperature (or overnight at 4° C.). The primary antibodies used (at 0.125 μg/well) were (1) rabbit anti-phospho-akt (Ser473) (Cell Signaling, Danvers, Mass.); (2) mouse anti-phospho-Erkl/2 (Cell Signaling, Danvers, Mass.); and (3) rabbit anti-phospho-ErbB2 (Abgent, San Diego, Calif.). The primary antibody was removed and the cells were washed 3 times with PBS. The secondary antibody (in PBS with 3% horse serum or PBS with 1% BSA, and 0.1% Triton® X-100) was then added for 1 hour at room temperature (or overnight at 4° C.) protected from light. The secondary antibodies used (at 0.2 μg/well) were Alexa 488 donkey anti-rabbit IgG (Invitrogen, Carlsbad, Calif.) and DyLight 649 goat anti-ms IgG (Pierce, Rockford, Ill.). The secondary antibody was removed and the cells were washed 3 times with PBS. Then 100 μL of PBS containing 200 ng/ml Hoechst 33342 nuclear stain (Invitrogen, H3570) (and if needed 1 ug/ml Cell Mask Blue cytoplasmic stain (Invitrogen, H34558) was added to the cells. The plates were covered and kept protected from light. The plates were then imaged.

[0203] Alternatively, we investigated anti-Her2 SMIP signal transduction activity in MDA-MB-361 cells as follows. MDA-MB-361 breast cancer cells, were plated in 6-well plate to 80-90% confluency (DMEM plus 10% FBS) and treated with anti-Her2 or control reagents for 24 hr with and without pretreatment with Heregulin (HRG—15 min.) or EGF (30 min.). For assay of total and phosphorylated Her2, cells were lysed, 50 ug total protein was fractionated using SDS-PAGE and transferred to nitrocellulose membranes using standard procedures. Western blot analysis used either rabbit anti-Her2 antibody (Cell Signaling Technologies), anti-pHer2_Y1248 (Upstate) or anti-Actin (Santa Cruz) as primary antibody and subsequently stained with HRP-conjugated anti-rabbit IgG. Peroxidase activity was measured using ECLplus2 kit (GE Healthcare) following manufacturer's protocols and exposed to film. As shown in FIG. **13**, HER033 induces HER2 phosphorylation.

[0204] To measure increased downstream phosphoprotein signal transduction, MDA-MB-361 breast cancer cells were plated in 96-well format and treated with anti-Her2 or control reagents for the concentrations and times (10 min to 24 hr) shown in FIG. **15**. Media was removed, cells washed with PBS, fixed with 4% paraformaldehyde, and permeabilized with 0.2% Triton 100/PBS. Cells were subsequently stained with either rabbit anti-pAKT (Cell Signaling Technologies), anti-pERK (Cellomics), anti-pS6K (Cell Signaling Technologies), or anti-p38MAPK (Cell Signaling Technologies). Following PBS wash (3×), cells were stained with secondary goat anti-rabbit IgG antibody labeled with ALEXA594. Cell fluorescence was quantified using Cellomics High Content assay at 594 nM.

[0205] Her067 (Her033) has agonistic activity (increased signaling) compared to trastuzumab (see Table 6). Moreover, Her067 and Her018 are generally a stronger inducer of Her2, Erk1/2, and Akt phosphorylation than trastuzumab. The increase was statistically significant as compared to the mock treatment when measured by the pairwise student T-test (<0.001).

TABLE 6

Induction of phosphorylation by HER018, HER067, Herceptin and Heregulin

MDA-MB-361(JL)	HER018	HER067	Herceptin	Heregulin
phospho-ErbB2	++	++	+	+
phospho-Erk1/2	+	++	+	+
phospho-Akt	+	+	+	++

Example 9

Cell Cycle Assay

[0206] To investigate the effect of the ErbB2 ECD binder on cell cycle in HERCEPTIN® sensitive and HERCEPTIN® resistant cells, each well of a 6 well plate was seeded with 2×10^5 cells (SKBR3 or BT474 (sensitive) or MDA-MB-453 or MDA-MB-361 (resistant) and incubated overnight at 37° C./5% CO_2. Cells were then treated with antibody or SMIP (at 10 μg/ml final) (in triplicate) and incubated for another 24 or 48 hours. After incubation, the cells were pulsed with 50 uM BrdU (Sigma) for 30 minutes at 37° C., the media was removed, and the cells were treated with trypsin and harvested in a FACS tube on ice. The cells were washed with PBS, fixed with 70% cold ethanol, and incubated on ice for 30 minutes. The ethanol was removed and then 2N HCl/0.5% Triton X-100 was added, and the cells were incubated for 30 minutes at room temperature (RT). The acid was removed and neutralized with 0.1 M $Na_2B_4O_7$ for 15 min at RT. The neutralization buffer was removed, FITC labeled anti-BrdU antibody was added (BD Bioscience) in PBS/0.5% TWEEN® 20/1% BSA, and the cells were incubated for 30 minutes at RT in the dark. The FITC dye was removed, the cells washed, and then DAPI nuclear stain (Invitrogen) and RNAse A (Qiagen) each at 1:1000 dilution was added and the cells were incubated 15 minutes in the dark and then analyzed by FACS. Statistical analysis of the data was performed using ANOVA and Student's t-test.

[0207] The results are presented in FIGS. **17** and **18**. We observed an increased number of cells in the G1 phase in HERCEPTIN® treated SKBR3, BT474 and MDA-MB-453 cells. Among cells treated with HER033 SMIP, we observed an increased number of cells in S phase in SKBR3 and BT474 cells.

Example 10

In Vivo Xenograft Assay

[0208] To investigate the effect of the ErbB2 binding molecules of the invention in vivo, we tested the molecules in three mouse models.

[0209] SCID/Beige Mouse Model

[0210] Female (6-7 week old) Beige SCID mice (Beige SCID CB-17/IcrHsd-Prkdcscid-Lystbg) were obtained from Harlan Sprague Dawley, N.J. Virus free MDA-MB-361 cells were thawed from a new vial and cultured to generate appropriate numbers. Cells were grown to near confluency and had a viability of >90%. Cells were harvested, washed twice with sterile PBS, resuspended to 2×10^8 cells/ml, then combined with Matrigel 1:2. and kept on ice until injection.

[0211] Tumor Cell Implantation and Monitoring: Each mouse was injected with 100 μl of the cell/Matrigel suspension (1×10^7 cells) subcutaneously on the right flank. Mice were monitored daily for tumor growth. Tumors were established when they reached about 150 to about 300 mm^3 (Volume=½[length×(width)^2). Tumors developed in 100% of the implanted mice. Mice were sorted into groups according to tumor size, keeping means consistent among groups using LabCat software. Sorting occurred on day 0, which was the same day the mice received their first treatment.

[0212] Mice were monitored (i.e., weighed and tumors measured) two to three times weekly. Mice were sacrificed if ulceration of tumor occurred, extreme body weight loss (greater than or equal 20%), tumor exceeded about 1200 to about 1500 mm^3, or tumor inhibited mobility of a mouse. The study is continued for a total of about 60 days.

[0213] Treatment: Mice were sorted into three groups of 11 mice each. Treatment began on day 0 (about six days after cell implantation). Each mouse of a group received intraperitoneal treatments twice a week (for a total of five treatments), which were given in equimolar amounts (900 nM) of (1) SMIP HER067 (100 μg), (2) Herceptin (136 μg, positive control), or (3) human IgG (136 μg, negative control). Survival and tumor size was recorded two to three times weekly. Results were graphed (+/−SEM) and analyzed using Prism software (see FIGS. **21** and **22**).

[0214] BALB/c nu and nu/nu Mouse Models

[0215] Male BALB/c nu/nu (nude) mice (18-23 g) and female nu/nu (nude) mice (18-23 g) were obtained from Charles River Laboratories, Wilmington, Mass.

[0216] Subcutaneous BCL Xenografts:

[0217] Female, athymic nude mice were exposed to total body irradiation (400 rads) to further suppress their residual immune system and facilitate the establishment of xenografts. Three days later, the irradiated mice were injected subcutaneously (SC) with 1×10^7 MDA-MB-361 cells in Matrigel (Collaborative Biomedical Products, Belford, Mass., diluted 1:1 in culture medium) in the dorsal, right flank. When the tumors reached the mass of 0.1 to 0.25 g, the tumors were staged to ensure uniformity of the treatment groups. Male, athymic Balb/c nude mice were injected s.c. with 1×10^7 cells in the right flank. When tumors reached an average tumor mass of 0.1 to 0.25 g, the tumors were staged to ensure uniformity of the treatment groups. Mice were dosed with compounds (100 μg/mouse ip) on days 1, 4, 6, 8 and 11 (n=10 mice/treatment group). All compounds were administered ip. Tumors were measured at least once a week and their mass (±SEM) was calculated. Tumor mass for each treatment group was compared to that from the vehicle-treated group for statistical significance using ANOVA and subsequent pairwise comparisons to the vehicle-treated group using a one-tailed t-test with the error term for the t-test based on the pooled variance across all treatment groups. The results are shown in FIGS. **19** and **20**.

[0218] The preliminary results in vivo as shown in FIGS. **19-22** are inconclusive. A number of factors could contribute to the differences observed in the three mouse models and are being further investigated. For example, while not intending to be limiting, the different experiments were dosed differently (twice weekly as compared to every other day, which means the former dosing lasted over a longer period of time, the tumors in the vehicle control groups in some of the experiments did not grow particularly well, and the mouse backgrounds had differing effector functionality (i.e, the nu/nu nude mice have B cells and NK cells, while the SKID/Beige mice have macrophages and monocytes. Based on the in vitro and in vivo results taken as a whole, the anti-ErbB2 binding proteins are believed to be efficacious in treating tumors.

[0219] The specification is most thoroughly understood in light of the teachings of the references cited within the specification. The embodiments within the specification provide an illustration of embodiments of the invention and should not be construed to limit the scope of the invention. The skilled artisan readily recognizes that many other embodiments are encompassed by the invention. All publications and patents cited in this disclosure are incorporated by reference in their entirety. To the extent the material incorporated by reference contradicts or is inconsistent with this specification, the specification will supercede any such material. The citation of any references herein is not an admission that such references are prior art to the present invention.

[0220] Unless otherwise indicated, all numbers expressing quantities of ingredients, reaction conditions, and so forth used in the application, are to be understood as being modified in all instances by the term "about." Accordingly, unless otherwise indicated to the contrary, the numerical parameters are approximations and may vary depending upon the desired properties sought to be obtained by the present invention. At the very least, and not as an attempt to limit the application of the doctrine of equivalents, each numerical parameter should be construed in light of the number of significant digits and ordinary rounding approaches.

[0221] Unless otherwise indicated, the term "at least" preceding a series of elements is to be understood to refer to every element in the series. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein.

SEQUENCE TABLE

Her2_S1R2A_CS_1F7

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMHWVRQAPGQGLEWMGWINP
NSGGTNYAQKFQGWVTMTRDTSISTAYMELSRLRSDDTAVYYCARDSTMAPGAF
DIWGRGTLVTVSS
(SEQ ID NO: 1)

SEQUENCE TABLE-continued

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSVAPGQTARMTCGGNNIESKTVHWYQQKPGQAPVLVVYNDNVRP
SGIPARFSGSNSGNTATLTINRVEAGDEADYYCQVWDSSRDQGVFGGGTKLTVLGA
(SEQ ID NO: 2)

Her2_S1R2A_CS_1D11

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVQSGSEVRRPGSSVRVSCTASGDTSSSFTVNWLRQAPGQGLEWMGGITPM
FGTANYAQMFEDRVTITADEMELSGLTSEDTAVYFCATGPSDYVWGSYRFLDTWG
RGTTVTVSS
(SEQ ID NO: 3)

V_L with CDR1, CDR2 and CDR3 underlined
QAVLTQPSSVSAAPGQEVSISCSGARSNVGGNYVSWYQHLPGTAPKLLIYDNNKR
PSGMPDRFSGSKSGTSATLGITGVQTEDEADYYCATWDSSLSAVVFGGGTKLTVL
GA
(SEQ ID NO: 4)

Her2_S1R2C_CS_1D3

V_H with CDR1, CDR2 and CDR3 underlined
QVQLVQSGSEVRRPGSSVRISCTASGDTSSSFTVNWVRQAPGQGLEWMGGITPM
FGTANYAQVFEDRVTIIADEMELSGLTSEDTAVYFCATGPSDYVWGSYRFLDRWG
RGTLVTVSS
(SEQ ID NO: 5)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSAAPGQKVTISCSGGRSSIGNNYVSWYQHLPGTAPKLLIYDNNQRP
SGIPDRFSGSKSGTSATLGITGLQTGDEADYYCGTWDSSLSAVVFGGGTKVTVLGA
(SEQ ID NO: 6)

Her2_S1R2C_Cs_1H12

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYGMNWVRQAPGKGLEWVSYISSS
GNTIFYADSVKGRFTISRDSAKNSVSLQMNSLRDEDTAVYYCASYYSYYYGMDAW
GQGTMVTV
(SEQ ID NO: 7)

V_L with CDR1, CDR2 and CDR3 underlined
SYVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQQLPGTAPKLLIYSNNQRP
SGVPDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDYSLSGWVFGGGTKVTVLGA
(SEQ ID NO: 8)

Her2_S1R2A_CS_1D3

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVQSGAEVKKPGASVKVSCKASGYSFTAFYIHWVRQAPGQGLEYLGWIDPNT
GATKYAQRFQGRVIMTWDTSITTATMELSRLTSDDSAVYYCVRDLREWGYELSVE
YWGRGTLVTVSS
(SEQ ID NO: 9)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNYVYWYQQLPGTAPKLLIYRNNQRP
SGVPDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLSGWVFGGGTKLTVLGA
(SEQ ID NO: 10)

Her2_S1R3B2_BMV_1E1

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVETGGGVVQPGGSLSLSCAASGFTFSSYGMQWVRQAPGKGLEWVAFIRYD
GSSEYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCGRTLESSLWGKGT
LVTVSS
(SEQ ID NO: 11)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSAAPGQKVTISCSGSTSNIGNNYVSWYQQHPGKAPKLMIYDVSKRP
SGVPDRFSGSKSGNSASLDISGLQSEDEADYYCAAWDDSLSEFLFGTRTKLTVLGA
(SEQ ID NO: 12)

SEQUENCE TABLE-continued

Her2_S1R3C1_CS_1D3

V_H with CDR1, CDR2 and CDR3 underlined
QVQLQESGPGLVKPSQTLSLTCGISGDSVSSNSAAWNWIRQSPTRGLEWLGRTYY
RSSWYHNYAPSMNSRLTIIADTSKNQFSLQLNSVTPEDTAVYYCASGWAFDVWGR
GTLVTVSS
(SEQ ID NO: 13)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGSPGQSVTISCTGTSSDVGAYDFVSWYQQHPGKAPKLMIYEVNK
RPSGVPDRFSGSKSGNTASLTVSGLQAEDEADYYCSSYAGSKNLLFGGGTKLTVL
GA
(SEQ ID NO: 14)

Her2_S1R3B2_DP47_1E8

V_H with CDR1, CDR2 and CDR3 underlined
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGS
GGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARQSGADWYFDLW
GRGTLVTVSS
(SEQ ID NO: 15)

V_L with CDR1, CDR2 and CDR3 underlined
QAVLTQPSAVSGAPGQRVTISCTGTSSNIGTNYLVHWYQQRPGTAPQLLVSGNNT
RPSGVTDRFSVSKSATSASLAITGLQAEDEADYYCQTYDINLRVWVFGGGTKVTVL
GA
(SEQ ID NO: 16)

Her2_S1R3B2_BMV_1G2

V_H with CDR1, CDR2 and CDR3 underlined
QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYGISWVRQAPGQGLEWMGWISAY
NGNTNYAQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARVPGVSGSYPDY
YYMDVWGKGTLVTVSS
(SEQ ID NO: 17)

V_L with CDR1, CDR2 and CDR3 underlined
DIQMTQSPSTLSASIGDRVTITCRASEGIYHWLAWYQQKPGKAPKLLIYKASSLASG
APSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYSNYPLTFGGGTKLEIKRA
(SEQ ID NO: 18)

Her2_S1R3B2_BMV_1H5

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVQSGGGLVRPGGSLRLSCAASGFSFSDYYMTWIRQIPGKGLEWVAVIWNDG
SDRYYADSVKGRFTISRDNSKNTLFLQMSSLRDEDTALYYCVRGGPTASSGFDYW
GRGTLVTVSS
(SEQ ID NO: 19)

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYLQHPGKAPKLMIYEGSKR
PSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVLGA
(SEQ ID NO: 20)

Her2_S1R3C1_CS_1A6
V_H with CDR1, CDR2 and CDR3 underlined

EVQLVQSGAEVKKPGESLKISCKGFGYNFRSAWIGWVRQMPGKGLEWMGVIYPG
DSDVRYSPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCTRPVGQWVDSDYW
GKGTLVTVSS
(SEQ ID NO: 21)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGTPGQRVTISCSGSSSNIGTNTVNWYQQLPGTAPKLLIYTSNQRP
SGVPARFSASNSGTSASLAISGLRSEDEADYYCAAWDDKLSGAVFGGGTKLTVLGA
(SEQ ID NO: 22)

Her2_S1R3B2_DP47_1C9

V_H with CDR1, CDR2 and CDR3 underlined
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGS
GGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARWRPLLDYHFDQ
WGQGTMVTVSS
(SEQ ID NO: 23)

SEQUENCE TABLE-continued

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGTPGQTVTISCSGSSSNIGSSVVNWYQQFPGTAPKVLVYSNTQR
PSGVPDRFSGSRSGTSASLAISGLQSEDEADYYCLAWDASLNGWVFGGGTKLTVL
GA
(SEQ ID NO: 24)

Her2_S1R3B2_DP47_1E10

V_H with CDR1, CDR2 and CDR3 underlined
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGS
GGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGYSGYDDPDSW
GRGTTVTVSS
(SEQ ID NO: 25)

V_L with CDR1, CDR2 and CDR3 underlined
HVILTQPPSTSGTPGQTVTISCSGSSSNIGSHYVYWYQQLPGTAPKLLIYRNNQRPS
GVPDRFSGSKSGTSASLAISGLRSEDETDYYCAAWDDSLSGRVFGTGTKLTVLGA
(SEQ ID NO: 26)

Her2_S1R3C1_CS_1B10

V_H with CDR1, CDR2 and CDR3 underlined
QVQLQQSGAEVKKPGSSVKVSCKASGGTISNYAISWVRLAPGQGLEWMGSIVPLH
GTTNFAQKFQGRVTITADESTSTSYMEVNVLTYEDTAMYYCASLNWGYWGRGTLV
TVSS
(SEQ ID NO: 27)

V_L with CDR1, CDR2 and CDR3 underlined
NFMLTQPHSVSESPGKTVTISCTGSSGSIASNYVQWYQQRPDSAPTTVIYEDNRRS
SGVPDRFSGSIDSNSASLSISGLKTEDEADYYCQSYDSSGHVVFGGGTKLTVLGA
(SEQ ID NO: 28)

Her2_S1R3A1_BMV_1F3

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVESGEGLVKPGGSLRLSCTASGFTFRSYSLNWVRQAPGQGLEWVSSISSTS
TYIYYADSVKGRFTISRDDAKNTLYLQMNSLRAEDTAAYYCVRLGSGGGYFPDYW
GRGTLVTVSS
(SEQ ID NO: 29)

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPS
GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNHVVFGGGTKLTVLGA
(SEQ ID NO: 30)

Her2_S1R3B1_BMV_1G11

V_H with CDR1, CDR2 and CDR3 underlined
QVQLVQSGGGLVQPGGSLRLSCAASGFTFSTYAMSWARQAPGKGLEWVSSISGD
GGRILDADSAKGRFTISRDNSKNTLYLQMNGLRVEDTALYYCARADGNYWGRGTM
VTVSS
(SEQ ID NO: 31)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSK
RPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVLGA
(SEQ ID NO: 32)

Her2_S1R3A1_BMV_1G4

V_H with CDR1, CDR2 and CDR3 underlined
QVQLVESGAEVKKPGASVKVSCKASGYTFTSYDINWVRQAPGQRLEWMGWINAG
NGNTKYSQKFQGRVTITRDTSASTAYMELRSLRSDDTAVYYCARGRSYGHPYYFD
YWGQGTLVTVSS
(SEQ ID NO: 33)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSK
RPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVLGA
(SEQ ID NO: 34)

SEQUENCE TABLE-continued

Her2_S1R3B1_BMV_1H11

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVQSGGGLVKPGGSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAGIFYD
GGNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDRGYYYMDVW
GKGTTVTVSS
(SEQ ID NO: 35)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSGAPGQRVTISCTGRSSNIGAGHDVHWYQQLPGTAPKLLIYGDSN
RPSGVPDRFSGSRSGTSASLAITGLQAEDEADYYCQSYDSSLRGSVFGGGTKVTV
LGA
(SEQ ID NO: 36)

Her2_S1R3A1_CS_1B9

V_H with CDR1, CDR2 and CDR3 underlined
KVQLVQSGTEVKKPGESLKISCQGSGYRFSSDWIAWVRQMPGKGLEWMGIVYPG
DSDTRYSPSFQGQVTISADKSISTAYLQWSGLKASDTAKYYCARVQQAVGAKGYA
MDVWGKGTLVTVSS
(SEQ ID NO: 37)

V_L with CDR1, CDR2 and CDR3 underlined
QTVVIQEPSFSVSPGGTVTLTCGLSSGSVSTSYYPSWYRQTPGQAPHTLIHNTKIRS
SGVPDRFSGSILGNNAALTITGAQADDESDYYCLLYMGSGIYVFGGGTKLTVLGA
(SEQ ID NO: 38)

Her2_S1R3B1_BMV_1H9

V_H with CDR1, CDR2 and CDR3 underlined
QVQLQESGAGLVKPSGTLSLTCAVSGGSISSGNWWSWVRQPPGKGLEWIGEISHS
GSTNYNPSLKSRVTISVDKSKNQFSLNLSSVTAADTAVYYCARVRGTVGDTRGPDY
WGQGTLVTVSS
(SEQ ID NO: 39)

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPS
GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNHVVFGGGTKLTVLGA
(SEQ ID NO: 40)

Her2_S1R3A1_CS_1B10

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVQSGAEVKKPGASVRVSCKGSGNTFTGHYIHWVRQAPGQGLEWLGWIDPN
TGDIQYSENFKGSVTLTRDPSINSVFMDLIRLTSDDTAMYYCAREGAGLANYYYYGL
DVWGRGTMVTVSS
(SEQ ID NO: 41)

V_L with CDR1, CDR2 and CDR3 underlined
QTVVLQEPSFSVSPGGTVTLTCGLNFGSVSTAYYPSWYQQTPGQAPRTLIYGTNIR
SSGVPDRFSGSIVGNKAALTITGAQTEDESDYYCALYMGSGMLFGGGTKVTVLGA
(SEQ ID NO: 42)

Her2_S1R3B1_BMV_1C12

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYD
GSIKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARTGEYSGYDTSGY
SNWGQGTLVTVSS
(SEQ ID NO: 43)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQRLPGAAPQLLIYNNDQRP
SGIPDRFSGSKSGTSGSLVISGLQSEDEADYYCASWDDSLNGRVFGGGTKLTVLG
(SEQ ID NO: 44)

Her2_S1R3C1_BMV_1H11

V_H with CDR1, CDR2 and CDR3 underlined
GVQLVESGGGLVKPGGSLRLSCAASGFTFSSYNMNWVRQAPGKGLEWVSAISGS
GGSTYYADSVTGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDTSGWYGDGM
DVWGRGTLVTVSS
(SEQ ID NO: 45)

SEQUENCE TABLE-continued

V_L with CDR1, CDR2 and CDR3 underlined
DIQMTQSPSTLSASIGDRVTITCRASEGIYHWLAWYQQKPGKAPKLLIYKASSLASG
APSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYSNYPLTFGGGTKLEIKRA
(SEQ ID NO: 46)

Her2_S1R3B1_BMV_1A10

V_H with CDR1, CDR2 and CDR3 underlined
QMQLVQSGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISY
DGSIKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTGVYYCSKDRYSSGWYSS
DAFDIWGRGTMVTVSS
(SEQ ID NO: 47)

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPS
GIPDRFSGSSSGNTASLTITGAQAEDEADYYCHSRDSSGNHVLFGGGTKLTVLGA
(SEQ ID NO: 48)

Her2_S1R3A1_CS_1D11

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVQSGAEVKKPGESLKISCKGSGYTFTNHWIAWVRQMPGKGLEWMGIIYPGD
SETRYSPSFQGHVTISADKSISTAYLQWSTLKDSDSAMYFCVRQARGWDDGRAGY
YYSGMDAWGQGTLVTVSS
(SEQ ID NO: 49)

V_L with CDR1, CDR2 and CDR3 underlined
QAVVLQEPSFSVSPGGTVTLTCGLRSGSVSTSHYPSWYQQTPGQAPRTLIYSTNT
RSSGVPDRFSGSILGNKAALTITGAQADDESNYYCMLYMGSGMYVFGGGTKVTVL
GA
(SEQ ID NO: 50)

Her2_S1R3C1_DP47_1H1

V_H with CDR1, CDR2 and CDR3 underlined
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGS
GGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVSGSHFPFFDS
WGQGTMVTVSS
(SEQ ID NO: 51)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSVAPGQTARITCGGDKIGHKSVHWYQQKPGQAPVLLVYDDRKRPS
GIPERFSGSNSGNTATLTISRVEAGDEAAYHCQVWDRSSDPYVFGTGTKVTVLGA
(SEQ ID NO: 52)

Her2_S1R3A1_CS_1B12

V_H with CDR1, CDR2 and CDR3 underlined
QVQLVQSGAEVKKPGASVKVSCQASGYTFSGHYMHLVRQAPGQGLEWMGWIHP
TSGGTTYAQKFQGRVVMTRDTSISTAYMELSRLTSDDTAVYYCARMSQNYDAFDI
WGQGTMVTVSS
(SEQ ID NO: 53)

V_L with CDR1, CDR2 and CDR3 underlined
QAVLTQPSSVSGAPGQRVTISCTGSSSNIGAGYDVNWYQQFPGTAPKIIVYGDRPS
GAPDRFSGSKSGTSASLAITGLRAEDEADYYCQSWDSRLSSYVFGTGTKVTVLGA
(SEQ ID NO: 54)

Her2_S1R3B1_BMV_1H5

V_H with CDR1, CDR2 and CDR3 underlined
QVQLQESGGGVVQPGGSLRLSCAASGFTFSGYGMHWVRQAPGKGLEWVASVRN
DGSNTYYTDSVKDRFTISRDNTKNTLYLQMNSLRAEDTAVYYCAKSRRVMYGTSY
YFDYWGRGTLVTVSS
(SEQ ID NO: 55)

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPS
GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNHVVFGGGTKLTVLGA
(SEQ ID NO: 56)

Her2_S1R3A1_DP47_1A6

V_H with CDR1, CDR2 and CDR3 underlined
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGS

SEQUENCE TABLE-continued

GGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARDLGIDPLWSGYY
TPLDYWGRGTMVTVSS
(SEQ ID NO: 57)

V_L with CDR1, CDR2 and CDR3 underlined
HVILTQPPSASGTPGQRVTISCSGSSSNIGSNSVSWYQQLPGTAPKLLMYTNNQRP
SGVPDRFSGSKSGTSASLAISGLQSEDEADYYCATWDASLNTWVFGGGTKVTVLGA
(SEQ ID NO: 58)

Her2_S1R3B1_DP47_1E1

V_H with CDR1, CDR2 and CDR3 underlined
EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGS
GGSTYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGGSGSDYWGQ
GTMVTVSS
(SEQ ID NO: 59)

V_L with CDR1, CDR2 and CDR3 underlined
NFMLTQPHSVSGSPGKTVTISCTRSSGYIDSKYVQWYQQRPGSAPTTVIYEDNRRP
SGVPDRFSGSIDSNSASLTISGLETEDEADYYCQSYDDTNVVFGGGTKVTVLGA
(SEQ ID NO: 60)

Her2_S1R3B1_BMV_1A1

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVQSGAEVKEPGASVKVSCKASGYDFSNYGFSWVRQAPGQGLEWMGWISS
YNGYTNYAQRLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARDRGLGNWYF
DLWGQGTLVTVSS
(SEQ ID NO: 61)

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSK
RPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVLGA
(SEQ ID NO: 62)

Her2_S1R2A_CS_1F7

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSVAPGQTARMTCGGNNIESKTVHWYQQKPGQAPVLVVYNDNVRP
SGIPARFSGSNSGNTATLTINRVEAGDEADYYCQVWDSSRDQGVFGGGTKLTVL
(SEQ ID NO: 63)

Her2_S1R2A_CS_1D11

V_L with CDR1, CDR2 and CDR3 underlined
QAVLTQPSSVSAAPGQEVSISCSGARSNVGGNYVSWYQHLPGTAPKLLIYDNNKR
PSGMPDRFSGSKSGTSATLGITGVQTEDEADYYCATWDSSLSAVVFGGGTKLTVL
(SEQ ID NO: 64)

Her2_S1R2C_CS_1D3

V_H with CDR1, CDR2 and CDR3 underlined
QVQLVQSGSEVRRPGSSVRISCTASGDTSSSFTVNWVRQAPGQGLEWMGGITPM
FGTANYAQVFEDRVTIIADEMELSGLTSEDTAVYFCATGPSDYVWGSYRFLDNWG
RGTLVTVSS
(SEQ ID NO: 65)

Her2_S1R2C_CS_1D3

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSAAPGQKVTISCSGGRSSIGNNYVSWYQHLPGTAPKLLIYDNNQRP
SGIPDRFSGSKSGTSATLGITGLQTGDEADYYCGTWDSSLSAVVFGGGTKVTVL
(SEQ ID NO: 66)

Her2_S1R2C_CS_1H12

V_H with CDR1, CDR2 and CDR3 underlined
EVQLVETGGGLVQPGGSLRLSCAASGFTFSSYGMNWVRQAPGKGLEWVSYISSS
GNTIFYADSVKGRFTISRDSAKNSVSLQMNSLRDEDTAVYYCASYYSYYYGMDAW
GQGTMVTVSS
(SEQ ID NO: 67)

Her2_S1R2C_CS_1H12

V_L with CDR1, CDR2 and CDR3 underlined
SYVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQQLPGTAPKLLIYSNNQRP

SEQUENCE TABLE-continued

SGVPDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDYSLSGWVFGGGTKVTVL
(SEQ ID NO: 68)

Her2_S1R2A_CS_1D3

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNYVYWYQQLPGTAPKLLIYRNNQRP
SGVPDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLSGWVFGGGTKLTVL
(SEQ ID NO: 69)

Her2_S1R3B2_BMV_1E1

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSAAPGQKVTISCSGSTSNIGNNYVSWYQQHPGKAPKLMIYDVSKRP
SGVPDRFSGSKSGNSASLDISGLQSEDEADYYCAAWDDSLSEFLFGTRTKLTVL
(SEQ ID NO: 70)

Her2_S1R3C1_CS_1D3

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGSPGQSVTISCTGTSSDVGAYDFVSWYQQHPGKAPKLMIYEVNK
RPSGVPDRFSGSKSGNTASLTVSGLQAEDEADYYCSSYAGSKNLLFGGGTKLTVL
(SEQ ID NO: 71)

Her2_S1R3B2_DP47_1E8

V_L with CDR1, CDR2 and CDR3 underlined
QAVLTQPSAVSGAPGQRVTISCTGTSSNIGTNYLVHWYQQRPGTAPQLLVSGNNT
RPSGVTDRFSVSKSATSASLAITGLQAEDEADYYCQTYDINLRVWVFGGGTKVTVL
(SEQ ID NO: 72)

Her2_S1R3B2_BMV_1G2

V_L with CDR1, CDR2 and CDR3 underlined
DIQMTQSPSTLSASIGDRVTITCRASEGIYHWLAWYQQKPGKAPKLLIYKASSLASG
APSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYSNYPLTFGGGTKLEIK
(SEQ ID NO: 73)

Her2_S1R3B2_BMV_1H5

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYLQHPGKAPKLMIYEGSKR
PSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL
(SEQ ID NO: 74)

Her2_S1R3C1_CS_1A6

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGTPGQRVTISCSGSSSNIGTNTVNWYQQLPGTAPKLLIYTSNQRP
SGVPARFSASNSGTSASLAISGLRSEDEADYYCAAWDDKLSGAVFGGGTKLTVL
(SEQ ID NO: 75)

Her2_S1R3B2_DP47_1C9

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGTPGQTVTISCSGSSSNIGSSVVNWYQQFPGTAPKVLVYSNTQR
PSGVPDRFSGSRSGTSASLAISGLQSEDEADYYCLAWDASLNGWVFGGGTKLTVL
(SEQ ID NO: 76)

Her2_S1R3B2_DP47_1E10

V_L with CDR1, CDR2 and CDR3 underlined
HVILTQPPSTSGTPGQTVTISCSGSSSNIGSHYVYWYQQLPGTAPKLLIYRNNQRPS
GVPDRFSGSKSGTSASLAISGLRSEDETDYYCAAWDDSLSGRVFGTGTKLTVL
(SEQ ID NO: 77)

Her2_S1R3C1_CS_1B10

V_L with CDR1, CDR2 and CDR3 underlined
NFMLTQPHSVSESPGKTVTISCTGSSGSIASNYVQWYQQRPDSAPTTVIYEDNRRS
SGVPDRFSGSIDSNSASLSISGLKTEDEADYYCQSYDSSGHVVFGGGTKLTVL
(SEQ ID NO: 78)

SEQUENCE TABLE-continued

Her2_S1R3A1_BMV_1F3

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPS
GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNHVVFGGGTKLTVL
(SEQ ID NO: 79)

Her2_S1R3B1_BMV_1G11

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSK
RPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL
(SEQ ID NO: 80)

Her2_S1R3A1_BMV_1G4

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSK
RPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL
(SEQ ID NO: 81)

Her2_S1R3B1_BMV_1H11

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSGAPGQRVTISCTGRSSNIGAGHDVHWYQQLPGTAPKLLIYGDSN
RPSGVPDRFSGSRSGTSASLAITGLQAEDEADYYCQSYDSSLRGSVFGGGTKVTVL
(SEQ ID NO: 82)

Her2_S1R3A1_CS_1B9

V_L with CDR1, CDR2 and CDR3 underlined
QTVVIQEPSFSVSPGGTVTLTCGLSSGSVSTSYYPSWYRQTPGQAPHTLIHNTKIRS
SGVPDRFSGSILGNNAALTITGAQADDESDYYCLLYMGSGIYVFGGGTKLTVL
(SEQ ID NO: 83)

Her2_S1R3B1_BMV_1H9

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPS
GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNHVVFGGGTKLTVL
(SEQ ID NO: 84)

Her2_S1R3A1_CS_1B10

V_L with CDR1, CDR2 and CDR3 underlined
QTVVLQEPSFSVSPGGTVTLTCGLNFGSVSTAYYPSWYQQTPGQAPRTLIYGTNIR
SSGVPDRFSGSIVGNKAALTITGAQTEDESDYYCALYMGSGMLFGGGTKVTVL
(SEQ ID NO: 85)

Her2_S1R3B1_BMV_1C12

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQRLPGAAPQLLIYNNDQRP
SGIPDRFSGSKSGTSGSLVISGLQSEDEADYYCASWDDSLNGRVFGGGTKLTVL
(SEQ ID NO: 86)

Her2_S1R3C1_BMV_1H11

V_L with CDR1, CDR2 and CDR3 underlined
DIQMTQSPSTLSASIGDRVTITCRASEGIYHWLAWYQQKPGKAPKLLIYKASSLASG
APSRFSGSGSGTDFTLTISSLQPDDFATYYCQQYSNYPLTFGGGTKLEIK
(SEQ ID NO: 87)

Her2_S1R3B1_BMV_1A10

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPS
GIPDRFSGSSSGNTASLTITGAQAEDEADYYCHSRDSSGNHVLFGGGTKLTVL
(SEQ ID NO: 88)

SEQUENCE TABLE-continued

Her2_S1R3A1_CS_1D11

V_L with CDR1, CDR2 and CDR3 underlined
QAVVLQEPSFSVSPGGTVTLTCGLRSGSVSTSHYPSWYQQTPGQAPRTLIYSTNT
RSSGVPDRFSGSILGNKAALTITGAQADDESNYYCMLYMGSGMYVFGGGTKVTVL
(SEQ ID NO: 89)

Her2_S1R3C1_DP47_1H1

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPPSVSVAPGQTARITCGGDKIGHKSVHWYQQKPGQAPVLLVYDDRKRPS
GIPERFSGSNSGNTATLTISRVEAGDEAAYHCQVWDRSSDPYVFGTGTKVTVL
(SEQ ID NO: 90)

Her2_S1R3A1_CS_1B12

V_L with CDR1, CDR2 and CDR3 underlined
QAVLTQPSSVSGAPGQRVTISCTGSSSNIGAGYDVNWYQQFPGTAPKIIVYGDRPS
GAPDRFSGSKSGTSASLAITGLRAEDEADYYCQSWDSRLSSYVFGTGTKVTVL
(SEQ ID NO: 91)

Her2_S1R3B1_BMV_1H5

V_L with CDR1, CDR2 and CDR3 underlined
SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPS
GIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSRDSSGNHVVFGGGTKLTVL
(SEQ ID NO: 92)

Her2_S1R3A1_DP47_1A6

V_L with CDR1, CDR2 and CDR3 underlined
HVILTQPPSASGTPGQRVTISCSGSSSNIGSNSVSWYQQLPGTAPKLLMYTNNQRP
SGVPDRFSGSKSGTSASLAISGLQSEDEADYYCATWDASLNTWVFGGGTKVTVL
(SEQ ID NO: 93)

Her2_S1R3B1_DP47_1E1

V_L with CDR1, CDR2 and CDR3 underlined
NFMLTQPHSVSGSPGKTVTISCTRSSGYIDSKYVQWYQQRPGSAPTTVIYEDNRRP
SGVPDRFSGSIDSNSASLTISGLETEDEADYYCQSYDDTNVVFGGGTKVTVL
(SEQ ID NO: 94)

Her2_S1R3B1_BMV_1A1

V_L with CDR1, CDR2 and CDR3 underlined
QSVLTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMIYEGSK
RPSGVSNRFSGSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVL
(SEQ ID NO 95)

Her2_S1R2A_CS_1F7

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTCCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAG
TGAAGGTCTCCTGCAAGGCTTCTGGATACACCTTCACCGGCTACTATATGCACT
GGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGGATCAACCC
TAACAGTGGTGGCACAAACTATGCACAGAAGTTTCAGGGCTGGGTCACCATGA
CCAGGGACACGTCCATCAGCACAGCCTACATGGAGCTGAGCAGGCTGAGATCT
GACGACACGGCCGTGTATTACTGTGCGAGAGATTCTACTATGGCCCCAGGTGC
TTTTGATATCTGGGGCCGAGGCACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 96)

Her2_S1R2A_CS_1F7

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCACCCTCGGTGTCAGTGGCCCCAGGACAGACGG
CCAGGATGACCTGTGGGGGAAACAACATTGAAAGTAAAACTGTGCATTGGTACC
AGCAGAAGCCGGGCCAGGCCCCTGTGCTGGTCGTCTACAATGATAACGTCCGG
CCCTCAGGGATCCCTGCGCGATTCTCTGGCTCCAACTCCGGCAACACGGCCAC
CCTGACCATCAACAGGGTCGAAGCCGGGGATGAGGCCGACTATTATTGTCAGG
TGTGGGACTCCAGTAGAGATCAAGGGGTATTCGGCGGAGGGACCAAGCTGAC
CGTC
(SEQ ID NO: 97)

SEQUENCE TABLE-continued

Her2_S1R2A_CS_1D11

V_H with CDR1, CDR2 and CDR3 underlined
GGAGGCCTGGGTCCTCGGTGAGGGTCTCCTGCACGGCTTCTGGAGACACCTC
CAGCAGCTTTACCGTCAACTGGCTGCGACAGGCCCCTGGACAAGGTCTTGAGT
GGATGGGAGGGATCACCCCTATGTTTGGCACTGCAAACTACGCACAGATGTTC
GAGGACAGAGTCACGATAACCGCGGACGAAATGGAACTGAGTGGCCTGACATC
TGAGGACACGGCCGTGTATTTTTGTGCGACAGGCCCCTCCGATTACGTTTGGG
GGAGTTATCGTTTCCTTGACACCTGGGGGCGGGGGACCACGGTCACCGTCTCG
AGT
(SEQ ID NO: 98)

Her2_S1R2A_CS_1D11

V_L with CDR1, CDR2 and CDR3 underlined
CAGGCTGTGCTGACTCAGCCGTCCTCAGTGTCTGCGGCCCCAGGACAGGAGG
TCTCCATCTCCTGCTCTGGAGCCAGATCCAACGTTGGGGGTAATTATGTTTCCT
GGTACCAACACCTCCCAGGAACAGCCCCCAAACTCCTCATTTATGACAATAATA
AGCGACCCTCAGGGATGCCTGACCGATTCTCTGGCTCCAAGTCTGGCACGTCA
GCCACCCTGGGCATCACCGGAGTCCAGACTGAGGACGAGGCCGATTATTACTG
CGCAACATGGGATAGCAGCCTGAGCGCTGTGGTCTTCGGCGGAGGGACCAAG
CTGACCGTCCTA
(SEQ ID NO: 99)

Her2_S1R2C_CS_1D3

V_H with CDR1, CDR2 and CDR3 underlined
CAGGTGCAGCTGGTGCAGTCTGGGTCTGAGGTGAGGAGGCCTGGGTCCTCGG
TGAGGATCTCCTGCACGGCTTCTGGAGACACCTCCAGCAGCTTTACCGTCAACT
GGGTGCGACAGGCCCCTGGACAAGGTCTTGAGTGGATGGGAGGGATCACCCC
TATGTTTGGCACTGCAAACTACGCACAGGTGTTCGAGGACAGAGTCACAATAAT
CGCGGACGAGATGGAACTGAGTGGCCTGACATCTGAGGACACGGCCGTGTATT
TCTGTGCGACAGGCCCCTCCGATTACGTTTGGGGGAGTTATCGTTTCCTTGACA
ACTGGGGCAGGGGCACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 100)

Her2_S1R2C_CS_1D3

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCACCCTCAGTGTCTGCGGCCCCAGGGCAGAAGGT
CACCATCTCCTGCTCTGGAGGCAGGTCCAGCATTGGGAATAATTATGTGTCCTG
GTATCAACACCTCCCAGGAACAGCCCCCAAACTCCTCATCTATGACAATAATCA
GCGACCCTCAGGGATTCCTGACCGATTCTCTGGCTCCAAGTCTGGCACGTCAG
CCACCCTGGGCATCACCGGACTCCAGACTGGGGACGAGGCCGATTATTACTGC
GGAACATGGGATAGCAGCCTGAGTGCTGTGGTGTTTGGCGGAGGGACCAAGG
TCACCGTCCTA
(SEQ ID NO: 101)

Her2_S1R2C_CS_1H12

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGGTGGAGACTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGAACT
GGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTTTCATACATTAGTAGT
TCTGGTAATACCATATTCTACGCAGACTCTGTGAAGGGCCGATTCACCATCTCC
AGAGACAGTGCCAAGAATTCAGTGTCTCTGCAGATGAACAGCCTGAGAGACGA
GGACACGGCTGTGTATTACTGTGCTTCCTACTACTCCTACTACTACGGTATGGA
CGCCTGGGGCCAGGGGACAATGGTCACCGTCTCGAGTTCGAGT
(SEQ ID NO: 102)

Her2_S1R2C_CS_1H12

V_L with CDR1, CDR2 and CDR3 underlined
TCTGGGACCCCCGGGCAGAGGGTCACCATCTCTTGTTCTGGAAGCAGCTCCAA
CATCGGAAGTAATACTGTAAACTGGTACCAGCAGCTCCCAGGAACGGCCCCCA
AACTCCTCATCTATAGTAATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCT
CTGGCTCCAAGTCTGGCACCTCAGCCTCCCTGGCCATCAGTGGGCTGCGGTCC
GAGGATGAGGCTGATTATTACTGTGCAGCATGGGATTACAGCCTGAGTGGTTG
GGTGTTCGGCGGAGGGACCAAGGTCACCGTCCTA
(SEQ ID NO: 103)

Her2_S1R2A_CS_1D3

V_H with CDR1, CDR2 and CDR3 underlined
GAAGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAG

SEQUENCE TABLE-continued

TGAAGGTCTCCTGCAAGGCTTCTGGGTACAGCTTCACCGCCTTCTATATTCACT
GGGTGCGACAGGCCCCTGGACAAGGCCTTGAGTATTTGGGATGGATCGACCCT
AATACTGGTGCCACAAAATATGCACAGCGCTTTCAGGGCAGGGTCATCATGACC
TGGGACACGTCCATCACCACAGCCACCATGGAACTGAGCAGGCTGACGTCTGA
CGACTCGGCCGTCTACTACTGTGTGAGAGATTTGCGGGAGTGGGGCTACGAAT
TGTCCGTTGAGTATTGGGGCAGAGGAACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 104)

Her2_S1R2A_CS_1D3

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCACCCTCAGCGTCTGGGACCCCCGGGCAGAGGG
TCACCATCTCTTGTTCTGGAAGCAGCTCCAACATCGGAAGTAATTATGTATACTG
GTACCAGCAGCTCCCAGGAACGGCCCCCAAACTCCTCATCTATAGGAATAATCA
GCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAG
CCTCCCTGGCCATCAGTGGGCTCCGGTCCGAGGATGAGGCTGATTATTACTGT
GCAGCATGGGATGACAGCCTGAGTGGTTGGGTGTTCGGCGGAGGGACCAAGC
TGACCGTCCTA
(SEQ ID NO: 105)

Her2_S1R3B2_BMV_1E1

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGGTGGAGACTGGGGGAGGCGTGGTCCAGCCTGGGGGGTCC
CTGAGCCTCTCCTGTGCAGCGTCTGGATTCACCTTCAGTAGCTATGGCATGCAG
TGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCGTTTATACGGT
ACGATGGAAGTAGTGAATACTATGCAGACTCCGTGAAGGGCCGATTCACCATCT
CCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTG
AGGACACGGCTGTGTATTACTGTGGAAGAACGCTGGAGTCTAGTTTGTGGGGC
AAGGGAACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 106)

Her2_S1R3B2_BMV_1E1

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGTTGACGCAGCCGCCCTCAGTGTCTGCGGCCCCAGGACAGAAGGT
CACCATTTCCTGCTCTGGAAGCACCTCCAACATTGGGAATAATTATGTCTCCTG
GTACCAACAGCACCCAGGCAAAGCCCCCAAACTCATGATTTATGATGTCAGTAA
GCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCAACTCAG
CCTCCCTGGACATCAGTGGGCTCCAGTCTGAGGATGAGGCTGATTATTACTGT
GCAGCATGGGATGACAGCCTGAGTGAATTTCTCTTCGGAACTAGGACCAAGCT
GACCGTCCTA
(SEQ ID NO: 107)

Her2_S1R3C1_CS_1D3

V_H with CDR1, CDR2 and CDR3 underlined
CAGGTGCAGCTGCAGGAGTCGGGTCCAGGACTGGTGAAGCCCTCGCAGACCT
TGTCACTCACCTGTGGCATCTCCGGGGACAGTGTCTCTAGCAACAGTGCTGCTT
GGAACTGGATCAGGCAGTCCCCAACGAGAGGCCTTGAGTGGCTGGGAAGGAC
ATATTACAGGTCCAGTTGGTATCATAACTATGCACCTTCTATGAACAGTCGATTA
ACCATCATCGCAGACACATCCAAAAACCAGTTCTCTTTGCAACTGAACTCTGTG
ACTCCCGAGGACACGGCTGTATATTACTGTGCAAGCGGGTGGGCCTTTGATGT
CTGGGGCAGGGGAACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 108)

Her2_S1R3C1_CS_1D3

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCACCCTCCGCGTCCGGGTCTCCTGGACAGTCAGT
CACCATCTCCTGCACTGGAACCAGCAGTGACGTTGGTGCTTATGACTTTGTCTC
CTGGTACCAACAGCACCCTGGCAAAGCCCCCAAACTCATGATTTATGAGGTCAA
TAAGCGGCCCTCAGGGGTCCCTGATCGCTTCTCTGGCTCCAAGTCTGGCAACA
CGGCCTCCCTGACCGTCTCTGGGCTCCAGGCTGAGGATGAGGCTGATTATTAC
TGCAGCTCATATGCAGGCAGCAAGAATTTGCTTTTCGGCGGAGGGACCAAGCT
GACCGTCCTA
(SEQ ID NO: 109)

Her2_S1R3B2_DP47_1E8

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGCAGCTATGCCATGAGCT
GGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGG
TAGTGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCT
CCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCC

SEQUENCE TABLE-continued

GAGGACACGGCCGTGTATTACTGTGCGAGACAGTCGGGCGCGGACTGGTACTT
CGATCTCTGGGGCCGAGGCACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 110)

Her2_S1R3B2_DP47_1E8

V_L with CDR1, CDR2 and CDR3 underlined
CAGGCTGTGCTGACTCAGCCGTCCGCAGTTTCTGGGGCCCCAGGGCAGAGGG
TCACCATCTCCTGCACTGGGACCAGCTCCAACATCGGGACAAACTATCTTGTAC
ACTGGTATCAGCAACGTCCAGGAACAGCCCCCCAACTCCTCGTCTCTGGTAAC
AACACTCGACCCTCTGGGGTCACTGACCGGTTCTCTGTCTCCAAGTCTGCCACT
TCAGCCTCCCTGGCCATCACTGGGCTCCAGGCTGAGGATGAGGCTGATTATTA
CTGCCAGACCTATGACATCAACTTGAGGGTTTGGGTGTTCGGCGGAGGGACCA
AGGTCACCGTCCTA
(SEQ ID NO: 111)

Her2_S1R3B2_BMV_1G2

V_H with CDR1, CDR2 and CDR3 underlined
CAGGTGCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGAAGCCTGGGTCCTCGG
TGAAGGTCTCCTGCAAGGCTTCTGGTTACACCTTTACCAGCTATGGTATCAGCT
GGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGATGGATCAGCGC
TTACAATGGTAACACAAACTATGCACAGAAGCTCCAGGGCAGAGTCACCATGAC
CACAGACACATCCACGAGCACAGCCTACATGGAGCTGAGGAGCCTGAGATCTG
ACGACACGGCCGTGTATTACTGTGCGAGAGTCCCGGGCGTAAGTGGGAGCTAT
CCAGACTACTACTACATGGACGTCTGGGGCAAGGGAACCCTGGTCACCGTCTC
CTCA
(SEQ ID NO: 112)

Her2_S1R3B2_BMV_1G2

V_L with CDR1, CDR2 and CDR3 underlined
GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTATTGGAGACAGA
GTCACCATCACCTGCCGGGCCAGTGAGGGTATTTATCACTGGTTGGCCTGGTA
TCAGCAGAAGCCAGGGAAAGCTCCTAAACTCCTGATCTATAAGGCCTCTAGTTT
AGCCAGTGGGGCCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGATTTCA
CTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAAC
AATATAGTAATTATCCGCTCACTTTCGGCGGAGGGACCAAGCTGGAGATCAAA
(SEQ ID NO: 113)

Her2_S1R3B2_BMV_1H5

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGGTGCAGTCTGGGGGAGGCTTGGTCAGGCCTGGAGGGTCCC
TGAGACTCTCCTGTGCAGCCTCGGGATTCTCCTTCAGTGACTACTACATGACCT
GGATCCGCCAGATTCCAGGGAAGGGGCTGGAGTGGGTGGCAGTTATATGGAAT
GATGGAAGTGATAGATACTATGCAGACTCCGTGAAGGGCCGATTCACCATTTCC
AGAGACAATTCCAAGAACACGCTGTTTCTGCAAATGAGCAGCCTGAGAGACGA
GGACACGGCTCTATATTACTGTGTGAGAGGGGGACCAACAGCTTCAAGCGGAT
TTGACTACTGGGGCCGAGGCACCCTGGTCACCGTCTCGAG
(SEQ ID NO: 114)

Her2_S1R3B2_BMV_1H5

V_L with CDR1, CDR2 and CDR3 underlined
TCGTCTGAGCTGACTCAGCCTGCCTCCGTGTCTGGGTCTCCTGGACAGTCGAT
CACCATCTCCTGCACTGGAACCAGCAGTGACGTTGGTGGTTATAACTATGTCTC
CTGGTACCTACAACACCCAGGCAAAGCCCCCAAACTCATGATTTATGAGGGCA
GTAAGCGGCCCTCAGGGGTTTCTAATCGCTTCTCTGGCTCCAAGTCTGGCAAC
ACGGCCTCCCTGACAATCTCTGGGCTCCAGGCTGAGGACGAGGCTGATTATTA
CTGCAGCTCATATACAACCAGGAGCACTCGAGTTTTCGGCGGAGGGACCAAGC
TGACCGTCCTA
(SEQ ID NO: 115)

Her2_S1R3C1_CS_1A6

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGGTGCAGTCTGGGGCAGAGGTGAAAAAGCCCGGGGAGTCTC
TGAAGATCTCCTGTAAGGGTTTTGGATACAATTTTCGCAGCGCCTGGATCGGCT
GGGTGCGCCAGATGCCCGGCAAAGGCCTGGAGTGGATGGGGGTCATCTATCC
TGGTGACTCTGATGTCAGATACAGTCCGTCCTTCCAAGGCCAGGTCACCATCTC
AGCCGACAAGTCCATCAGTACCGCCTACCTGCAGTGGAGCAGCCTGAAAGCCT
CGGACACCGCCATGTATTATTGTACGAGACCCGTAGGGCAGTGGGTGGACTCT
GACTATTGGGGCAAGGGAACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 116)

SEQUENCE TABLE-continued

Her2_S1R3C1_CS_1A6

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGTTGACGCAGCCGCCCTCAGCGTCTGGGACCCCCGGACAGAGGG
TCACCATCTCTTGTTCTGGAAGCAGCTCCAACATCGGAACTAATACTGTGAACT
GGTACCAGCAGCTTCCAGGAACGGCCCCCAAACTCCTCATCTATACTAGTAATC
AGCGGCCCTCAGGGGTCCCTGCCCGCTTCTCTGCCTCCAACTCTGGCACCTCA
GCCTCCCTGGCCATCAGTGGGCTCCGGTCCGAGGATGAGGCTGATTATTATTG
TGCAGCGTGGGATGACAAGTTGAGTGGTGCGGTGTTCGGCGGAGGGACCAAG
CTGACCGTCCTA
(SEQ ID NO: 117)

Her2_S1R3B2_DP47_1C9

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGCAGCTATGCCATGAGCT
GGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGG
TAGTGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCT
CCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCC
GAGGACACGGCCGTGTATTACTGTGCGAGATGGAGGCCTCTTCTAGACTACCA
CTTTGACCAATGGGGCCAAGGGACAATGGTCACCGTCTCGAGT
(SEQ ID NO: 118)

Her2_S1R3B2_DP47_1C9

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCACCCTCAGCGTCTGGGACCCCCGGACAGACGGT
AACAATCTCTTGTTCTGGAAGCAGCTCCAACATCGGAAGTAGTGTTGTTAATTG
GTACCAGCAGTTCCCAGGAACGGCCCCCAAAGTCCTCGTCTATAGTAACACTCA
GCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAGGTCTGGCACCTCAG
CCTCCCTGGCCATCAGTGGGCTCCAGTCTGAGGATGAGGCTGATTATTACTGTT
TAGCATGGGATGCCAGCCTGAATGGTTGGGTGTTCGGCGGAGGGACCAAGCT
GACCGTCCTA
(SEQ ID NO: 119)

Her2_S1R3B2_DP47_1E10

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGCAGCTATGCCATGAGCT
GGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGG
TAGTGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCT
CCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCC
GAGGACACGGCCGTGTATTACTGTGCGAGAGGATACAGTGGCTACGATGACCC
TGACTCCTGGGGGAGAGGGACCACGGTCACCGTCTCGAGT
(SEQ ID NO: 120)

Her2_S1R3B2_DP47_1E10

V_L with CDR1, CDR2 and CDR3 underiined
CACGTTATACTGACTCAACCGCCCTCAACGTCTGGGACCCCCGGGCAGACGGT
CACCATCTCTTGTTCTGGGAGCAGCTCCAACATCGGAAGTCATTATGTATACTG
GTACCAGCAGCTCCCAGGAACGGCCCCCAAACTCCTCATCTATAGGAATAATCA
GCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAG
CCTCCCTGGCCATCAGTGGGCTCCGGTCCGAGGATGAGACTGATTATTACTGT
GCAGCATGGGATGACAGCCTGAGTGGTCGAGTCTTCGGAACTGGGACCAAGCT
GACCGTCCTA
(SEQ ID NO: 121)

Her2_S1R3C1_CS_1B10

V_H with CDR1, CDR2 and CDR3 underlined
CAGGTACAGCTGCAGCAGTCAGGGGCTGAGGTGAAGAAGCCTGGGTCCTCGG
TGAAGGTCTCCTGCAAGGCTTCTGGAGGCACCATCAGCAACTATGCTATCAGTT
GGGTGCGGCTGGCCCCTGGACAAGGTCTTGAGTGGATGGGAAGTATCGTCCC
TCTTCATGGGACAACAAACTTCGCACAGAAATTCCAGGGCAGAGTCACGATCAC
CGCGGACGAGTCCACGAGCACATCCTACATGGAGGTGAACGTCCTGACATATG
AAGACACGGCGATGTATTATTGTGCGTCTCTCAATTGGGGCTACTGGGGCCGG
GGCACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 122)

Her2_S1R3C1_CS_1B10

V_L with CDR1, CDR2 and CDR3 underlined
AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGAGTCTCCGGGGAAGACGGT

SEQUENCE TABLE-continued

AACCATCTCCTGCACCGGCAGTAGTGGCAGCATTGCCAGCAACTATGTGCAGT
GGTACCAGCAGCGCCCGGACAGTGCCCCCACCACTGTGATCTATGAGGATAAT
CGAAGATCCTCTGGAGTCCCTGATCGGTTCTCTGGCTCCATCGACAGCTCCTC
CAACTCTGCCTCCCTCAGCATCTCTGGACTGAAGACTGAGGACGAGGCTGACT
ACTACTGTCAGTCCTATGATAGTAGCGGTCATGTGGTCTTCGGCGGAGGGACC
AAGCTGACCGTCCTA
(SEQ ID NO: 123)

Her2_S1R3A1_BMV_1F3

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGGTGGAGTCTGGGGAAGGCCTGGTCAAGCCTGGGGGGTCCC
TGAGACTCTCCTGTACAGCCTCTGGATTCACCTTCAGGAGTTATAGCTTGAACT
GGGTCCGCCAGGCTCCAGGGCAGGGGCTGGAGTGGGTCTCATCCATTAGTAG
TACTAGTACTTACATATACTACGCAGACTCGGTGAAGGGCCGATTCACCATCTC
CAGAGACGACGCCAAGAACACACTGTATCTGCAAATGAACAGCCTGAGAGCCG
AAGACACAGCTGCATATTACTGTGTTAGACTGGGATCTGGTGGGGGATATTTTC
CTGACTACTGGGGCAGGGGCACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 124)

Her2_S1R3A1_BMV_1F3

V_L with CDR1, CDR2 and CDR3 underlined
TCGTCTGAGCTGACTCAGGACCCTGCTGTGTCTGTGGCCTTGGGACAGACAGT
CAGGATCACATGCCAAGGAGACAGCCTCAGAAGCTATTATGCAAGCTGGTACC
AGCAGAAGCCAGGACAGGCCCCTGTACTTGTCATCTATGGTAAAAACAACCGG
CCCTCAGGGATCCCAGACCGATTCTCTGGCTCCAGCTCAGGAAACACAGCTTC
CTTGACCATCACTGGGGCTCAGGCGGAAGATGAGGCTGACTATTACTGTAACT
CCCGGGACAGCAGTGGTAACCATGTGGTATTCGGCGGAGGGACCAAGCTGAC
CGTCCTA
(SEQ ID NO: 125)

Her2_S1R3B1_BMV_1G11

V_H with CDR1, CDR2 and CDR3 underlined
CAGGTGCAGCTGGTGCAGTCTGGGGGAGGCTTGGTCCAGCCGGGGGGGTCC
CTGAGACTCTCCTGTGCAGCCTCTGGATTCACGTTTAGTACCTATGCCATGAGT
TGGGCCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAAGTATTAGTG
GTGATGGTGGAAGAATTCTCGATGCAGACTCCGCGAAGGGCCGGTTCACCATC
TCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACGGCCTGAGAGTC
GAGGACACGGCCCTTTATTACTGTGCGAGAGCGGACGGTAACTACTGGGGCAG
GGGGACAATGGTCACCGTCTCTTCA
(SEQ ID NO: 126)

Her2_S1R3B1_BMV_1G11

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCTGCCTCCGTGTCTGGGTCTCCTGGACAGTCGAT
CACCATCTCCTGCACTGGAACCAGCAGTGACGTTGGTGGTTATAACTATGTCTC
CTGGTACCAACAACACCCAGGCAAAGCCCCCAAACTCATGATTTATGAGGGCA
GTAAGCGGCCCTCAGGGGTTTCTAATCGCTTCTCTGGCTCCAAGTCTGGCAAC
ACGGCCTCCCTGACAATCTCTGGGCTCCAGGCTGAGGACGAGGCTGATTATTA
CTGCAGCTCATATACAACCAGGAGCACTCGAGTTTTCGGCGGAGGGACCAAGC
TGACCGTCCTA
(SEQ ID NO: 127)

Her2_S1R3A1_BMV_1G4

V_H with CDR1, CDR2 and CDR3 underlined
CAGGTGCAGCTGGTGGAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAG
TGAAGGTCTCCTGCAAGGCTTCTGGATACACCTTCACCAGTTATGATATCAACT
GGGTGCGACAGGCCCCCGGACAAAGGCTTGAGTGGATGGGATGGATCAACGC
TGGCAATGGTAACACAAAATATTCACAGAAGTTCCAGGGCAGAGTCACCATTAC
CAGGGACACATCCGCGAGCACAGCCTACATGGAGCTGAGGAGCCTGAGATCT
GACGACACGGCCGTGTATTACTGTGCGAGAGGGAGGAGCTATGGCCACCCGT
ACTACTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 128)

Her2_S1R3A1_BMV_1G4

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCTGCCTCCGTGTCTGGGTCTCCTGGACAGTCGAT
CACCATCTCCTGCACTGGAACCAGCAGTGACGTTGGTGGTTATAACTATGTCTC
CTGGTACCAACAACACCCAGGCAAAGCCCCCAAACTCATGATFVATGAGGGCA
GTAAGCGGCCCTCAGGGGTTTCTAATCGCTTCTCTGGCTCCAAGTCTGGCAAC
ACGGCCTCCCTGACAATCTCTGGGCTCCAGGCTGAGGACGAGGCTGATTATTA

SEQUENCE TABLE-continued

CTGCAGCTCATATACAACCAGGAGCACTCGAGTTTTCGGCGGAGGGACCAAGC
TGACCGTCCTA
(SEQ ID NO: 129)

Her2_S1R3B1_BMV_1H11

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGGTGCAGTCTGGGGGAGGCCTGGTCAAGCCTGGGGGGTCCC
TGAGACTCTCCTGTGCAGCGTCTGGATTCACCTTCAGTAGCTATGGGATGCACT
GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGGTATTTTTTAT
GATGGAGGTAATAAATACTATGCAGACTCCGTGAAGGGCCGATTCACCATCTCC
AGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGAG
GACACGGCTGTGTATTACTGTGCGAGAGATAGGGGCTACTACTACATGGACGT
CTGGGGCAAAGGGACCACGGTCACCGTCTCCTCA
(SEQ ID NO: 130)

Her2_S1R3B1_BMV_1H11

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGTTGACGCAGCCGCCCTCAGTGTCTGGGGCCCCAGGACAGAGGG
TCACCATCTCCTGCACTGGGAGAAGCTCCAACATCGGGGCGGGTCATGATGTA
CACTGGTACCAGCAACTTCCAGGAACAGCCCCCAAACTCCTCATCTATGGTGAC
AGCAATCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAGGTCTGGCAC
CTCAGCCTCCCTGGCCATCACTGGGCTCCAGGCTGAAGATGAGGCTGATTATT
ACTGCCAGTCCTATGACAGCAGCCTGAGGGGTTCGGTATTCGGCGGAGGGAC
CAAGGTCACCGTCCTA
(SEQ ID NO: 131)

Her2_S1R3A1_CS_1B9

V_H with CDR1, CDR2 and CDR3 underlined
AAGGTGCAGCTGGTGCAGTCTGGGACAGAGGTGAAAAAGCCCGGGGAGTCTC
TGAAGATCTCCTGTCAGGGTTCTGGATACAGGTTTAGTAGTGACTGGATTGCCT
GGGTGCGCCAGATGCCCGGGAAAGGCCTGGAGTGGATGGGGATTGTCTATCC
TGGTGACTCTGATACCAGATATAGCCCGTCCTTCCAAGGCCAAGTCACCATCTC
AGCCGACAAGTCCATCAGTACTGCCTACCTGCAGTGGAGCGGCCTGAAGGCCT
CGGACACCGCCAAGTATTACTGTGCGAGAGTGCAACAGGCAGTGGGAGCTAAA
GGTTATGCTATGGACGTCTGGGGCAAGGGAACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 132)

Her2_S1R3A1_CS_1B9

V_L with CDR1, CDR2 and CDR3 underlined
CAGACTGTGGTGATCCAGGAGCCATCGTTCTCAGTGTCCCCTGGAGGGACAGT
CACACTCACTTGTGGCTTGAGCTCTGGCTCAGTCTCTACCAGTTACTACCCCAG
CTGGTACCGGCAGACCCCAGGCCAGGCTCCACACACACTCATTCACAACACAA
AGATTCGCTCCTCTGGGGTCCCTGATCGCTTCTCTGGCTCCATCCTTGGGAACA
ATGCTGCCCTCACCATCACGGGGGCCCAGGCAGATGATGAATCTGATTATTACT
GTCTTTTGTATATGGGTAGCGGCATTTACGTGTTCGGCGGAGGGACCAAGCTG
ACCGTCCTA
(SEQ ID NO: 133)

Her2_S1R3B1_BMV_1H9

V_H with CDR1, CDR2 and CDR3 underlined
CAGGTGCAGCTGCAGGAGTCGGGCGCAGGACTGGTGAAGCCTTCGGGGACCC
TGTCCCTCACCTGCGCTGTCTCTGGTGGCTCCATCAGCAGTGGTAACTGGTGG
AGTTGGGTCCGCCAGCCCCCAGGGAAGGGGCTGGAGTGGATTGGGGAAATCT
CTCATAGTGGGAGCACCAACTACAACCCGTCCCTCAAGAGTCGAGTCACCATAT
CAGTAGACAAGTCCAAGAACCAGTTCTCCCTGAACCTGAGTTCTGTGACCGCC
GCAGACACGGCCGTGTATTACTGTGCGAGAGTAAGGGGTACGGTGGGGGATA
CACGGGGACCTGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 134)

Her2_S1R3B1_BMV_1H9

V_L with CDR1, CDR2 and CDR3 underlined
TCGTCTGAGCTGACTCAGGACCCTGCTGTGTCTGTGGCCTTGGGACAGACAGT
CAGGATCACATGCCAAGGAGACAGCCTCAGAAGCTATTATGCAAGCTGGTACC
AGCAGAAGCCAGGACAGGCCCCTGTACTTGTCATCTATGGTAAAAACAACCGG
CCCTCAGGGATCCCAGACCGATTCTCTGGCTCCAGCTCAGGAAACACAGCTTC
CTTGACCATCACTGGGGCTCAGGCGGAAGATGAGGCTGACTATTACTGTAACT
CCCGGGACAGCAGTGGTAACCATGTGGTATTCGGCGGAGGGACCAAGCTGAC
CGTCCTA
(SEQ ID NO: 135)

SEQUENCE TABLE-continued

Her2_S1R3A1_CS_1B10

V_H with CDR1, CDR2 and CDR3 underlined
GAAGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAAGCCTGGGGCCTCAG
TGAGGGTCTCCTGCAAGGGTTCTGGAAACACCTTCACCGGCCACTACATCCAC
TGGGTGCGACAGGCCCCTGGACAAGGACTTGAGTGGCTGGGATGGATCGACC
CTAACACTGGTGACATACAGTATTCAGAAAACTTTAAGGGCTCGGTCACCTTGA
CCAGGGACCCATCCATCAACTCAGTCTTCATGGACCTGATCAGGCTGACATCTG
ACGACACGGCCATGTATTACTGTGCGAGAGAAGGTGCCGGGCTCGCCAACTAC
TATTACTACGGTCTGGACGTCTGGGGCCGAGGGACAATGGTCACCGTCTCGAGT
(SEQ ID NO: 136)

Her2_S1R3A1_CS_1B10

V_L with CDR1, CDR2 and CDR3 underlined
CAGACTGTGGTGCTCCAGGAGCCTTCGTTCTCAGTGTCCCCTGGGGGGACAGT
CACACTCACTTGTGGCTTGAACTTTGGCTCAGTCTCTACTGCTTACTACCCCAG
TTGGTACCAGCAGACCCCAGGCCAAGCTCCACGCACGCTCATCTACGGCACAA
ATATTCGTTCCTCTGGGGTCCCGGATCGCTTCTCTGGCTCCATCGTAGGGAACA
AAGCTGCCCTCACCATCACGGGGGCCCAGACAGAAGATGAGTCTGATTATTATT
GTGCGCTGTATATGGGTAGTGGCATGCTCTTCGGCGGCGGGACCAAGGTCACC
GTCCTA
(SEQ ID NO: 137)

Her2_S1R3B1_BMV_1C12

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGGTGCAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACT
GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATA
TGATGGAAGTATTAAATACTATGCAGACTCCGTGAAGGGCCGATTCACCATCTC
CAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCTGA
GGACACGGCTGTGTATTACTGTGCGCGAACTGGTGAATATAGTGGCTACGATA
CGAGTGGTTACAGCAATTGGGGCCAAGGCACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 138)

Her2_S1R3B1_BMV_1C12

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCACCCTCAGCGTCTGGGACCCCCGGGCAGAGGG
TCACCATCTCTTGTTCTGGAAGCAGCTCCAACATCGGGAGTAACACTGTAAACT
GGTACCAGCGACTCCCAGGAGCGGCCCCCCAACTCCTCATCTACAATAATGAC
CAGCGGCCCTCAGGGATCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTC
AGGCTCCCTGGTCATCAGTGGGCTCCAGTCTGAAGATGAGGCTGATTACTACT
GTGCGTCATGGGATGACAGTCTGAATGGTCGGGTGTTCGGCGGAGGGACCAA
GCTGACCGTCCTA
(SEQ ID NO: 139)

Her2_S1R3C1_BMV_1H11

V_H with CDR1, CDR2 and CDR3 underlined
GGGGTGCAGCTGGTGGAGTCTGGGGGAGGCCTGGTCAAGCCTGGGGGGTCC
CTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATAACATGAAC
TGGGTCCGCCAGGCTCCAGGGAAGGGACTGGAGTGGGTCTCAGCTATTAGTG
GTAGTGGTGGTAGCACATACTACGCAGACTCCGTGACGGGCCGGTTCACCATC
TCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCC
GAGGACACGGCCGTATATTACTGTGCGAAAGATACCAGTGGCTGGTACGGGGA
CGGTATGGACGTCTGGGGCCGGGGAACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 140)

Her2_S1R3C1_BMV_1H11

V_L with CDR1, CDR2 and CDR3 underlined
GACATCCAGATGACCCAGTCTCCTTCCACCCTGTCTGCATCTATTGGAGACAGA
GTCACCATCACCTGCCGGGCCAGTGAGGGTATTTATCACTGGTTGGCCTGGTA
TCAGCAGAAGCCAGGGAAAGCCCCTAAACTCCTGATCTATAAGGCCTCTAGTTT
AGCCAGTGGGGCCCCATCAAGGTTCAGCGGCAGTGGATCAGGGACAGATTTCA
CTCTCACCATCAGCAGCCTGCAGCCTGATGATTTTGCAACTTATTACTGCCAAC
AATATAGTAATTATCCGCTCACTTTCGGCGGAGGGACCAAGCTGGAGATCAAA
(SEQ ID NO: 141)

Her2_S1R3B1_BMV_1A10

V_H with CDR1, CDR2 and CDR3 underlined
CAGATGCAGCTGGTGCAGTCTGGGGGAGGCGTGGTCCAGCCTGGGAGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTCAGTAGCTATGGCATGCACT

SEQUENCE TABLE-continued

GGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCAGTTATATCATA
TGATGGAAGTATTAAATACTATGCAGACTCCGTGAAGGGCCGATTCACCATCTC
CAGAGACAATTCCAAGAACACACTGTATCTACAAATGAACAGCCTGAGAGCCGA
GGACACGGGCGTTTATTACTGTTCGAAAGATCGCTATAGCAGTGGCTGGTACA
GCTCCGATGCTTTTGATATTTGGGGCCGAGGGACAATGGTCACCGTCTCGAGT
(SEQ ID NO: 142)

Her2_S1R3B1_BMV_1A10

V_L with CDR1, CDR2 and CDR3 underlined
TCTGAGCTGACTCAGGACCCTGCTGTGTCTGTGGCCTTGGGACAGACAGTCAG
GATCACATGCCAAGGAGACAGCCTCAGAAGCTATTATGCAAGCTGGTACCAGC
AGAAGCCAGGACAGGCCCCTGTACTTGTCATCTATGGTAAAAACAACCGGCCC
TCAGGGATCCCAGACCGATTCTCTGGCTCCAGCTCAGGAAACACAGCTTCCTT
GACCATCACTGGGGCTCAGGCGGAAGATGAGGCTGACTATTACTGTCATTCCC
GGGACAGCAGTGGTAACCATGTGCTTTTCGGCGGAGGGACCAAGCTGACCGTC
CTA
(SEQ ID NO: 143)

Her2_S1R3A1_CS_1D11

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGGTGCAGTCTGGGGCAGAGGTGAAAAAGCCCGGAGAGTCTC
TGAAGATCTCCTGTAAGGGCTCTGGATACACCTTTACCAACCACTGGATCGCCT
GGGTGCGCCAGATGCCCGGGAAAGGCCTGGAGTGGATGGGCATCATCTATCC
TGGTGACTCTGAAACGAGGTACAGCCCGTCCTTCCAAGGCCACGTCACCATCT
CAGCCGACAAGTCCATCAGTACCGCCTATTTGCAGTGGAGCACCCTGAAGGAC
TCGGACTCCGCCATGTACTTCTGTGTGAGACAGGCCCGTGGCTGGGACGACG
GACGGGCTGGATATTATTATTCCGGTATGGACGCCTGGGGCCAGGGAACCCTG
GTCACCGTCTCGAGT
(SEQ ID NO: 144)

Her2_S1R3A1_CS_1D11

V_L with CDR1, CDR2 and CDR3 underlined
CAGGCTGTGGTGCTCCAGGAGCCATCGTTCTCAGTGTCCCCTGGAGGGACAGT
CACACTCACCTGTGGCTTGCGCTCTGGGTCAGTCTCTACTAGTCACTACCCCAG
CTGGTACCAGCAGACCCCAGGCCAGGCTCCACGCACGCTCATTTACAGCACAA
ACACTCGCTCTTCTGGGGTCCCTGATCGCTTCTCTGGCTCCATCCTTGGGAACA
AAGCTGCCCTCACCATCACGGGGGCCCAGGCAGATGATGAATCTAATTATTACT
GTATGCTATACATGGGCAGTGGCATGTATGTGTTCGGCGGAGGGACCAAGGTC
ACCGTCCTA
(SEQ ID NO: 145)

Her2_S1R3C1_DP47_1H1

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGCAGCTATGCCATGAGCT
GGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGG
TAGTGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCT
CCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCC
GAGGACACGGCCGTGTATTACTGTGCGAGAGTCAGCGGGAGCCACTTTCCATT
CTTTGACTCCTGGGGCCAGGGGACAATGGTCACCGTCTCGAGT
(SEQ ID NO: 146)

Her2_S1R3C1_DP47_1H1

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCACCCTCGGTGTCAGTGGCCCCAGGACAGACGG
CCAGAATTACCTGTGGGGGAGACAAGATTGGACATAAAAGTGTGCATTGGTATC
AGCAGAAGCCAGGCCAGGCCCCTGTGTTGCTCGTCTATGATGATAGGAAGCGG
CCCTCAGGGATCCCTGAGCGATTCTCTGGCTCCAACTCTGGGAACACGGCCAC
CCTGACCATCAGCAGGGTCGAGGCCGGGGATGAGGCTGCCTATCACTGTCAG
GTGTGGGATAGAAGTAGTGACCCTTATGTCTTCGGAACTGGGACCAAGGTCAC
CGTCCTA
(SEQ ID NO: 147)

Her2_S1R3A1_CS_1B12

V_H with CDR1, CDR2 and CDR3 underlined
CAGGTGCAGCTGGTGCAATCTGGGGCTGAAGTGAAGAAGCCTGGGGCCTCAG
TGAAGGTCTCTTGTCAGGCTTCTGGATACACCTTCAGCGGGCACTATATGCACT
TGGTGCGACAGGCCCCTGGACAAGGGCTTGAGTGGATGGGGTGGATCCACCC
TACCAGTGGTGGCACAACCTATGCACAGAAGTTTCAGGGCCGGGTCGTTATGA
CCAGGGACACGTCCATCAGCACAGCCTACATGGAACTGAGTAGGCTGACATCT

SEQUENCE TABLE-continued

GACGACACGGCCGTGTATTACTGTGCAAGAATGTCCCAAAACTATGATGCTTTT
GATATCTGGGGCCAAGGGACAATGGTCACCGTCTCGAGT
(SEQ ID NO: 148)

Her2_S1R3A1_CS_1B12

V_L with CDR1, CDR2 and CDR3 underlined
CAGGCTGTGCTGACTCAGCCGTCCTCAGTGTCTGGGGCCCCAGGGCAGAGGG
TCACCATCTCCTGCACTGGGAGCAGCTCCAACATCGGGGCAGGTTATGATGTA
AACTGGTACCAACAATTTCCAGGAACAGCCCCCAAAATTATCGTCTATGGCGAT
CGGCCCTCAGGGGCCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGC
CTCCCTGGCAATCACTGGACTCCGGGCTGAGGATGAGGCTGATTATTACTGCC
AGTCCTGGGACAGTCGCCTGAGTAGTTATGTCTTCGGAACTGGGACCAAGGTC
ACCGTCCTA
(SEQ ID NO: 149)

Her2_S1R3B1_BMV_1H5

V_H with CDR1, CDR2 and CDR3 underlined
CAGGTGCAGCTGCAGGAGTCGGGGGGAGGCGTGGTCCAGCCTGGGGGGTCC
CTGAGACTCTCCTGTGCAGCGTCTGGATTCACCTTCAGTGGCTATGGCATGCAC
TGGGTCCGCCAGGCTCCAGGCAAGGGGCTGGAGTGGGTGGCATCTGTACGGA
ACGATGGAAGTAATACATACTACACAGACTCCGTGAAGGACCGATTCACCATCT
CCAGAGACAACACCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCC
GAGGACACGGCCGTATATTACTGTGCCAAGTCGAGAAGAGTGATGTATGGCAC
CTCCTATTACTTTGACTACTGGGGCAGAGGCACCCTGGTCACCGTCTCCTCA
(SEQ ID NO: 150)

Her2_S1R3B1_BMV_1H5

V_L with CDR1, CDR2 and CDR3 underlined
TCGTCTGAGCTGACTCAGGACCCTGCTGTGTCTGTGGCCTTGGGACAGACAGT
CAGGATCACATGCCAAGGAGACAGCCTCAGAAGCTATTATGCAAGCTGGTACC
AGCAGAAGCCAGGACAGGCCCCTGTACTTGTCATCTATGGTAAAAACAACCGG
CCCTCAGGGATCCCAGACCGATTCTCTGGCTCCAGCTCAGGAAACACAGCTTC
CTTGACCATCACTGGGGCTCAGGCGGAAGATGAGGCTGACTATTACTGTAACT
CCCGGGACAGCAGTGGTAACCATGTGGTATTCGGCGGAGGGACCAAGCTGAC
CGTCCTA
(SEQ ID NO: 151)

Her2_S1R3A1_DP47_1A6

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGCAGCTATGCCATGAGCT
GGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGG
TAGTGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCT
CCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCC
GAGGACACGGCCGTGTATTACTGTGCGAGAGATCTGGGAATAGACCCCCTTTG
GAGTGGTTATTACACACCCCTTGACTATTGGGGCCGAGGGACAATGGTCACCG
TCTCGAGT
(SEQ ID NO: 152)

Her2_S1R3A1_DP47_1A6

V_L with CDR1, CDR2 and CDR3 underlined
CACGTTATACTGACTCAACCGCCCTCAGCGTCTGGGACCCCCGGGCAGAGGGT
CACCATCTCTTGTTCTGGAAGCAGCTCCAACATCGGAAGTAATTCCGTTAGCTG
GTACCAGCAGCTCCCAGGAACGGCCCCCAAACTCCTCATGTATACTAACAATCA
GCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAG
CCTCCCTGGCCATCAGTGGGCTCCAGTCTGAGGATGAGGCTGATTATTACTGT
GCGACATGGGATGCCAGCCTGAATACTTGGGTGTTCGGCGGAGGGACCAAGG
TCACCGTCCTA
(SEQ ID NO: 153)

Her2_S1R3B1_DP47_1E1

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCC
TGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGCAGCTATGCCATGAGCT
GGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGG
TAGTGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCT
CCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCC
GAGGACACGGCCGTGTATTACTGTGCGAGAGGCGGGAGTGGGAGTGACTACT
GGGGCCAGGGGACAATGGTCACCGTCTCGAGT
(SEQ ID NO: 154)

SEQUENCE TABLE-continued

Her2_S1R3B1_DP47_1E1

V_L with CDR1, CDR2 and CDR3 underlined
AATTTTATGCTGACTCAGCCCCACTCTGTGTCGGGGTCTCCGGGGAAGACGGT
AACCATCTCCTGCACCCGCAGCAGTGGCTACATTGACAGCAAGTATGTGCAGT
GGTACCAGCAGCGCCCGGGCAGTGCCCCCACCACTGTGATCTATGAGGATAAC
CGAAGACCCTCTGGGGTCCCTGATCGGTTCTCTGGCTCCATCGACAGCTCCTC
CAACTCTGCCTCCCTCACCATCTCTGGACTGGAGACTGAGGACGAGGCTGACT
ATTACTGTCAGTCTTATGATGACACCAATGTGGTGTTCGGCGGAGGGACCAAG
GTCACCGTCCTA
(SEQ ID NO: 155)

Her2_S1R3B1_BMV_1A1

V_H with CDR1, CDR2 and CDR3 underlined
GAGGTCCAGCTGGTGCAGTCTGGAGCTGAGGTGAAGGAGCCTGGGGCCTCAG
TGAAGGTCTCCTGCAAGGCCTCTGGTTACGACTTTTCCAACTATGGTTTCAGCT
GGGTGCGCCAGGCCCCTGGACAAGGTCTTGAGTGGATGGGATGGATCAGCTC
TTATAATGGTTACACAAACTATGCACAGAGACTCCAGGGCAGAGTCACCATGAC
CACAGACACATCCACGAGCACAGCCTACATGGAGCTGAGGAGCCTGAGATCTG
ACGACACAGCTGTCTATTACTGTGCGAGAGATCGAGGACTTGGAAACTGGTACT
TCGATCTCTGGGGCCAAGGCACCCTGGTCACCGTCTCGAGT
(SEQ ID NO: 156)

Her2_S1R3B1_BMV_1A1

V_L with CDR1, CDR2 and CDR3 underlined
CAGTCTGTGCTGACTCAGCCTGCCTCCGTGTCTGGGTCTCCTGGACAGTCGAT
CACCATCTCCTGCACTGGAACCAGCAGTGACGTTGGTGGTTATAACTATGTCTC
CTGGTACCAACAACACCCAGGCAAAGCCCCCAAACTCATGATTTATGAGGGCA
GTAAGCGGCCCTCAGGGGTTTCTAATCGCTTCTCTGGCTCCAAGTCTGGCAAC
ACGGCCTCCCTGACAATCTCTGGGCTCCAGGCTGAGGACGAGGCTGATTATTA
CTGCAGCTCATATACAACCAGGAGCACTCGAGTTTTCGGCGGAGGGACCAAGC
TGACCGTCCTA

(SEQ ID NO: 157)

>HER018_CDS

atggattttcaagtgcagattttcagcttcctgctaatcagtgcttcagtcataatgtccagaggagatattcagatgaccc
agagcccgagcagcctgagcgcgagcgtgggcgatcgcgtgaccattacctgccgcgcgagccaggatgtgaac
accgcggtggcgtggtatcagcagaaaccgggcaaagcgccgaaactgctgatttatagcgcgagctttctgtatag
cggcgtgccgagccgctttagcggcagccgcagcggcaccgattttaccctgaccattagcagcctgcagccggaa
gattttgcgacctattattgccagcagcattataccaccccgccgacctttggccagggcaccaaagtggaaattaaa
cgcaccgggggtggaggctctggtggcggtggctctggcggaggtggatccggtggcggcggatctgaagtgcag
ctggtggaaagcggcggcggcctggtgcagccgggcggcagcctgcgcctgagctgcgcggcgagcggctttaa
cattaaagatacctatattcattgggtgcgccaggcgccgggcaaaggcctggaatgggtggcgcgcatttatccgac
caacggctatacccgctatgcggatagcgtgaaaggccgctttaccattagcgcggataccagcaaaaacaccgc
gtatctgcagatgaacagcctgcgcgcggaagatgccgcggtgtattattgcagccgctggggcggcgatggctttta
tgcgatggattattggggccagggcaccctggtgaccgtgagcagtgatcaggagcccaaatcttgtgacaaaactc
acacatctccaccgtgctcagcacctgaactcctgggtggaccgtcagtcttcctcttcccccaaaacccaaggaca
ccctcatgatctcccggacccctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttc
aactggtacgtggacggcgtggaggtgcataatgccaagacaaagccgcgggaggagcagtacaacagcacgt
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ctccgacggctccttcttcctctacagcaagctcaccgtggacaagagcaggtggcagcaggggaacgtcttctcatg
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(SEQ ID NO: 158)

>HER018_Protein_leader-stop

MDFQVQIFSFLLISASVIMSRGDIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAW
YQQKPGKAPKLLIYSASFLYSGVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHY
TTPPTFGQGTKVEIKRTGGGGSGGGGSGGGGSGGGGSEVQLVESGGGLVQPGG
SLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISA
DTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSSDQEPK
SCDKTHTSPPCSAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVK
FNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKAL
PAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNG
QPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS
LSLSPGK
(SEQ ID NO: 159)

SEQUENCE TABLE-continued

>HER018_2h7_Leader_CDS

atggattttcaagtgcagattttcagcttcctgctaatcagtgcttcagtcataatgtccagagga
(SEQ ID NO: 160)

>HER018_2h7_Leader_Protein

MDFQVQIFSFLLISASVIMSRG
(SEQ ID NO: 161)

>HER018_VL_CDS

Gatattcagatgacccagagcccgagcagcctgagcgcgagcgtgggcgatcgcgtgaccattacctgccgcgcg
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aaagtggaaattaaacgcacc
(SEQ ID NO: 162)

>HER018_VL_Protein

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYS
GVPSRFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIKRT
(SEQ ID NO: 163)

>HER018_G4Sx4_Linker_CDS

gggggtggaggctctggtggcggtggctctggcggaggtggatccggtggcggcggatct
(SEQ ID NO: 164)

>HER018_G4Sx4_Linker_Protein

GGGGSGGGGSGGGGSGGGGS
(SEQ ID NO: 165)

>HER018_VH_CDS

gaagtgcagctggtggaaagcggcggcggcctggtgcagccgggcggcagcctgcgcctgagctgcgcggcga
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(SEQ ID NO: 166)

>HER018_VH_Protein

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTN
GYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDY
WGQGTLVTVSS
(SEQ ID NO: 167)

>HER018_CSCS_Hinge_CDS

gagcccaaatcttgtgacaaaactcacacatctccaccgtgctca
(SEQ ID NO: 168)

>HER018_CSCS_Hinge_Protein
EPKSCDKTHTSPPCS
(SEQ ID NO: 169)

>HER018_Fc_Stop_CDS

gcacctgaactcctgggtggaccgtcagtcttcctcttcccccaaaacccaaggacaccctcatgatctcccggacc
cctgaggtcacatgcgtggtggtggacgtgagccacgaagaccctgaggtcaagttcaactggtacgtggacggcg
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(SEQ ID NO: 170)

SEQUENCE TABLE-continued

>HER018_Fc_Stop_Protein

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AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVL
DSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
(SEQ ID NO: 171)

>HER026_CDS

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(SEQ ID NO: 172)

>HER026_Protein_leader-stop

MEAPAQLLFLLLLWLPDTTGEVQLVQSGSEVRRPGSSVRVSCTASGDTSSSFTVN
WLRQAPGQGLEWMGGITPMFGTANYAQMFEDRVTITADEMELSGLTSEDTAVYFC
ATGPSDYVWGSYRFLDTWGRGTTVTVSSGGGGSGGGGSGGGGSAQAVLTQPSS
VSAAPGQEVSISCSGARSNVGGNYVSWYQHLPGTAPKLLIYDNNKRPSGMPDRFS
GSKSGTSATLGITGVQTEDEADYYCATWDSSLSAVVFGGGTKLTVLGDVREPKSS
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPGK
(SEQ ID NO: 173)

>HER027_CDS

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(SEQ ID NO: 174)

>HER027_Protein_leader-stop

MEAPAQLLFLLLLWLPDTTGQVQLVQSGSEVRRPGSSVRISCTASGDTSSSFTVN
WVRQAPGQGLEWMGGITPMFGTANYAQVFEDRVTIIADEMELSGLTSEDTAVYFC
ATGPSDYVWGSYRFLDNWGRGTLVTVSSGGGGSGGGGSGGGGSAQSVLTQPPS

SEQUENCE TABLE-continued

VSAAPGQKVTISCSGGRSSIGNNYVSWYQHLPGTAPKLLIYDNNQRPSGIPDRFSG
SKSGTSATLGITGLQTGDEADYYCGTWDSSLSAVVFGGGTKVTVLGDVREPKSSD
KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW
YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
(SEQ ID NO: 175)

>HER028_CDS

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(SEQ ID NO: 176)

>HER028_Protein_leader-stop

MEAPAQLLFLLLLWLPDTTGEVQLVQSGAEVKKPGASVKVSCKASGYSFTAFYIHW
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VYYCVRDLREWGYELSVEYWGRGTLVTVSSGGGGSGGGGSGGGGSAQSVLTQP
PSASGTPGQRVTISCSGSSSNIGSNYVYWYQQLPGTAPKLLIYRNNQRPSGVPDRF
SGSKSGTSASLAISGLRSEDEADYYCAAWDDSLSGWVFGGGTKLTVLGDVREPKS
SDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKF
NWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP
APIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQ
PENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSL
SLSPGK
(SEQ ID NO: 177)

>HER029_CDS

atggaagcaccagcgcagcttctcttcctcctgctactctggctcccagataccaccggtgaggtgcagctggtgcagt
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(SEQ ID NO: 178)

>HER029_Protein_leader-stop

MEAPAQLLFLLLLWLPDTTGEVQLVQSGAEVKKPGASVKVSCKASGYTFTGYYMH
WVRQAPGQGLEWMGWINPNSGGTNYAQKFQGWVTMTRDTSISTAYMELSRLRS
DDTAVYYCARDSTMAPGAFDIWGRGTLVTVSSGGGGSGGGGSGGGGSAQSVLT

SEQUENCE TABLE-continued

QPPSVSVAPGQTARMTCGGNNIESKTVHWYQQKPGQAPVLVVYNDNVRPSGIPA
RFSGSNSGNTATLTINRVEAGDEADYYCQVWDSSRDQGVFGGGTKLTVLGDVRE
PKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPE
VKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNK
ALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWES
NGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYT
QKSLSLSPGK
(SEQ ID NO: 179)

>HER030_CDS

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(SEQ ID NO: 180)

>HER030_Protein_leader-stop

MEAPAQLLFLLLLWLPDTTGEVQLVQSGGGLVRPGGSLRLSCAASGFSFSDYYMT
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ALYYCVRGGPTASSGFDYWGRGTLVTVSSGGGGSGGGGSGGGGSSELTQPASV
SGSPGQSITISCTGTSSDVGGYNYVSWYLQHPGKAPKLMIYEGSKRPSGVSNRFS
GSKSGNTASLTISGLQAEDEADYYCSSYTTRSTRVFGGGTKLTVLGDVREPKSSDK
THTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWY
VDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIE
KTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN
NYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLS
PGK
(SEQ ID NO: 181)

>HER031_CDS

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(SEQ ID NO: 182)

>HER031_Protein_leader-stop

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SEQUENCE TABLE-continued

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(SEQ ID NO: 183)

>HER032_CDS

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(SEQ ID NO: 184)

>HER032_Protein_leader-stop

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LSPGK
(SEQ ID NO: 185)

>HER033_CDS

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(SEQ ID NO: 186)

>HER033_Protein_leader-stop

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SEQUENCE TABLE-continued

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SEQ ID NO: 187)

>HER034_CDS

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(SEQ ID NO: 188)

>HER034_Protein_leader-stop

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(SEQ ID NO: 189)

>HER035_CDS

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(SEQ ID NO: 190)

>HER035_Protein_leader-stop

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SEQUENCE TABLE-continued

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(SEQ ID NO: 191)

>HER036_CDS

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(SEQ ID NO: 192)

>HER036_Protein_leader-stop

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(SEQ ID NO: 193)

>HER037_CDS

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(SEQ ID NO: 194)

>HER037_Protein_leader-stop

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SEQUENCE TABLE-continued

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(SEQ ID NO: 195)

>HER038_CDS

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(SEQ ID NO: 196)

>HER038_Protein_leader-stop

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(SEQ ID NO: 197)

>HER039_CDS

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(SEQ ID NO: 198)

>HER039_Protein_leader-stop

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SEQUENCE TABLE-continued

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(SEQ ID NO: 199)

>HER071_CDS

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(SEQ ID NO: 200)

>HER071_Protein_leader-stop

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(SEQ ID NO: 201)

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(SEQ ID NO: 202)

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SEQUENCE TABLE-continued

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(SEQ ID NO: 203)

>HER073_CDS

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(SEQ ID NO: 204)

>HER073_Protein_leader-stop

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(SEQ ID NO: 205)

>HER074_CDS

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(SEQ ID NO: 206)

>HER074_Protein_leader-stop

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SEQUENCE TABLE-continued

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(SEQ ID NO: 207)

>HER075_CDS

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(SEQ ID NO: 208)

>HER075_Protein_leader-stop

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(SEQ ID NO: 210)

>HER076_Protein_leader-stop

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SEQUENCE TABLE-continued

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AVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA
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(SEQ ID NO: 211)

>HER077_CDS

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SEQ ID NO: 212)

>HER077_Protein_leader-stop

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(SEQ ID NO: 213)

>HER078_CDS

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(SEQ ID NO: 214)

>HER078_Protein_leader-stop

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SEQUENCE TABLE-continued

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(SEQ ID NO: 215)

>HER079_CDS

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(SEQ ID NO: 216)

>HER079_Protein_leader-stop

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SEQ ID NO: 217)

>HER080_CDS

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(SEQ ID NO: 218)

>HER080_Protein_leader-stop

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SEQUENCE TABLE-continued

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(SEQ ID NO: 219)

>HER081_CDS

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(SEQ ID NO: 220)

>HER081_Protein_leader-stop

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(SEQ ID NO: 221)

>HER082_CDS

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(SEQ ID NO: 222)

>HER082_Protein_leader-stop

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SEQUENCE TABLE-continued

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(SEQ ID NO: 223)

>HER083_CDS

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(SEQ ID NO: 224)

>HER083_Protein_leader-stop

MEAPAQLLFLLLLWLPDTTGQVQLQESGAGLVKPSGTLSLTCAVSGGSISSGNWW
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AVYYCARVRGTVGDTRGPDYWGQGTLVTVSSGGGGSGGGGSGGGGSSELTQDP
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EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE
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SPGK
(SEQ NO: 225)

>HER084_CDS

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(SEQ ID NO: 226)

>HER084_Protein_leader-stop

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SGAPGQRVTISCTGRSSNIGAGHDVHWYQQLPGTAPKLLIYGDSNRPSGVPDRFS
GSRSGTSASLAITGLQAEDEADYYCQSYDSSLRGSVFGGGTKVTVLGDVREPKSS
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA

SEQUENCE TABLE-continued

PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
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LSPGK
SEQ ID NO: 227)

>HER085_CDS

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(SEQ Id NO: 228)

>HER085_Protein_leader-stop

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TAVYYCARGGSGSDYWGQGTMVTVSSGGGGSGGGGSGGGGSALNFMLTQPHS
VSGSPGKTVTISCTRSSGYIDSKYVQWYQQRPGSAPTTVIYEDNRRPSGVPDRFS
GSIDSSSNSASLTISGLETEDEADYYCQSYDDTNVVFGGGTKVTVLGDVREPKSSD
KTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW
YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPI
EKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPE
NNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSL
SPGK
SEQ ID NO: 229)

>HER086_CDS

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(SEQ ID NO: 230)

>HER086_Protein_leader-stop

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WVRQAPGKGLEWVSAISGSGGSTYYADSVTGRFTISRDNSKNTLYLQMNSLRAED
TAVYYCAKDTSGWYGDGMDVWGRGTLVTVSSGGGGSGGGGSGGGGSDIQMTQ
SPSTLSASIGDRVTITCRASEGIYHWLAWYQQKPGKAPKLLIYKASSLASGAPSRFS
GSGSGTDFTLTISSLQPDDFATYYCQQYSNYPLTFGGGTKLEIKRDVREPKSSDKT
HTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEK

SEQUENCE TABLE-continued

TISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN
YKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSP
GK
(SEQ ID NO: 231)

>HER087_CDS

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(SEQ ID NO: 232)

>HER087_Protein_leader-stop

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TAVYYCARVSGSHFPFFDSWGQGTMVTVSSGGGGSGGGGSGGGGSAQSVLTQP
PSVSVAPGQTARITCGGDKIGHKSVHWYQQKPGQAPVLLVYDDRKRPSGIPERFS
GSNSGNTATLTISRVEAGDEAAYHCQVWDRSSDPYVFGTGTKVTVLGDVREPKSS
DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPA
PIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQP
ENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLS
LSPGK
(SEQ ID NO: 233)

>HER_SMIPs_huVk3_Leader_CDS

atggaagcaccagcgcagcttctcttcctcctgctactctggctcccagataccaccggt
(SEQ ID NO: 234)

>HER_SMIPs_huVk3_Leader_Protein

MEAPAQLLFLLLLWLPDTTG
(SEQ ID NO: 235)

>HER_SMIPs_G4Sx3_Linker_CDS

ggaggcggcggttcaggcggaggtggctctggcggtggcggaagt
(SEQ ID NO: 236)

>HER_SMIPs_G4Sx3_Linker_Protein

GGGGSGGGGSGGGGS
(SEQ ID NO: 237)

>HER_SMIPs_SCCP_Hinge_CDS

gagcccaaatcttctgacaaaactcacacatgcccaccgtgccca
(SEQ ID NO: 238)

>HER_SMIPs_SCCP_Hinge_Protein

EPKSSDKTHTCPPCP
(SEQ ID NO: 239)

SEQUENCE TABLE-continued

>HER_SMIP_Fc-Stop_CDS

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gagcctctccctgtctccgggtaaatga
(SEQ ID NO: 240)

>HER_SMIP_Fc_Stop_Protein

DVREPKSSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSH
EDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAV
EWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH
NHYTQKSLSLSPGK
(SEQ ID NO: 241)

SEQUENCE LISTING

<160> NUMBER OF SEQ ID NOS: 276

<210> SEQ ID NO 1
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 1

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Trp Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Ser Thr Met Ala Pro Gly Ala Phe Asp Ile Trp Gly Arg
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 2
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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 2

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Met Thr Cys Gly Gly Asn Asn Ile Glu Ser Lys Thr Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asn Asp Asn Val Arg Pro Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Asn Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Arg Asp Gln
85 90 95

Gly Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 3
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<212> TYPE: PRT
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<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 3

Glu Val Gln Leu Val Gln Ser Gly Ser Glu Val Arg Arg Pro Gly Ser
1 5 10 15

Ser Val Arg Val Ser Cys Thr Ala Ser Gly Asp Thr Ser Ser Ser Phe
20 25 30

Thr Val Asn Trp Leu Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Thr Pro Met Phe Gly Thr Ala Asn Tyr Ala Gln Met Phe
50 55 60

Glu Asp Arg Val Thr Ile Thr Ala Asp Glu Met Glu Leu Ser Gly Leu
65 70 75 80

Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Thr Gly Pro Ser Asp
85 90 95

Tyr Val Trp Gly Ser Tyr Arg Phe Leu Asp Thr Trp Gly Arg Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> SEQ ID NO 4
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 4

Gln Ala Val Leu Thr Gln Pro Ser Ser Val Ser Ala Ala Pro Gly Gln
1 5 10 15

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Glu Val Ser Ile Ser Cys Ser Gly Ala Arg Ser Asn Val Gly Gly Asn
20 25 30

Tyr Val Ser Trp Tyr Gln His Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Met Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Val Gln
65 70 75 80

Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Ser Ser Leu
85 90 95

Ser Ala Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 5
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 5

Gln Val Gln Leu Val Gln Ser Gly Ser Glu Val Arg Arg Pro Gly Ser
1 5 10 15

Ser Val Arg Ile Ser Cys Thr Ala Ser Gly Asp Thr Ser Ser Ser Phe
20 25 30

Thr Val Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Thr Pro Met Phe Gly Thr Ala Asn Tyr Ala Gln Val Phe
50 55 60

Glu Asp Arg Val Thr Ile Ile Ala Asp Glu Met Glu Leu Ser Gly Leu
65 70 75 80

Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Thr Gly Pro Ser Asp
85 90 95

Tyr Val Trp Gly Ser Tyr Arg Phe Leu Asp Arg Trp Gly Arg Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 6
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 6

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln
1 5 10 15

Lys Val Thr Ile Ser Cys Ser Gly Gly Arg Ser Ser Ile Gly Asn Asn
20 25 30

Tyr Val Ser Trp Tyr Gln His Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

-continued

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Ile Tyr Asp Asn Asn Gln Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65                  70                  75                  80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Trp Asp Ser Ser Leu
85                  90                  95

Ser Ala Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Ala
100                 105                 110


<210> SEQ ID NO 7
<211> LENGTH: 117
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 7

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20                  25                  30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35                  40                  45

Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile Phe Tyr Ala Asp Ser Val
50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Ser Ala Lys Asn Ser Val Ser
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85                  90                  95

Ala Ser Tyr Tyr Ser Tyr Tyr Tyr Gly Met Asp Ala Trp Gly Gln Gly
100                 105                 110

Thr Met Val Thr Val
115


<210> SEQ ID NO 8
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 8

Ser Tyr Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20                  25                  30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35                  40                  45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Tyr Ser Leu
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85 90 95

Ser Gly Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 9
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 9

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Ala Phe
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Tyr Leu
35 40 45

Gly Trp Ile Asp Pro Asn Thr Gly Ala Thr Lys Tyr Ala Gln Arg Phe
50 55 60

Gln Gly Arg Val Ile Met Thr Trp Asp Thr Ser Ile Thr Thr Ala Thr
65 70 75 80

Met Glu Leu Ser Arg Leu Thr Ser Asp Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Val Arg Asp Leu Arg Glu Trp Gly Tyr Glu Leu Ser Val Glu Tyr Trp
100 105 110

Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 10
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 10

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Arg Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85 90 95

Ser Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 11

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<211> LENGTH: 115
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 11

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Phe Ile Arg Tyr Asp Gly Ser Ser Glu Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Gly Arg Thr Leu Glu Ser Ser Leu Trp Gly Lys Gly Thr Leu Val Thr
100 105 110

Val Ser Ser
115

<210> SEQ ID NO 12
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 12

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln
1 5 10 15

Lys Val Thr Ile Ser Cys Ser Gly Ser Thr Ser Asn Ile Gly Asn Asn
20 25 30

Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met
35 40 45

Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Asn Ser Ala Ser Leu Asp Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85 90 95

Ser Glu Phe Leu Phe Gly Thr Arg Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 13
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

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<400> SEQUENCE: 13

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Gly Ile Ser Gly Asp Ser Val Ser Ser Asn
20 25 30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Thr Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Ser Trp Tyr His Asn Tyr Ala
50 55 60

Pro Ser Met Asn Ser Arg Leu Thr Ile Ile Ala Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Ser Gly Trp Ala Phe Asp Val Trp Gly Arg Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 14
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 14

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ala Tyr
20 25 30

Asp Phe Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Asn Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
85 90 95

Lys Asn Leu Leu Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 15
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 15

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

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20                  25                  30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35                  40                  45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85                  90                  95

Ala Arg Gln Ser Gly Ala Asp Trp Tyr Phe Asp Leu Trp Gly Arg Gly
100                 105                 110

Thr Leu Val Thr Val Ser Ser
115


<210> SEQ ID NO 16
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 16

Gln Ala Val Leu Thr Gln Pro Ser Ala Val Ser Gly Ala Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asn Ile Gly Thr Asn
20                  25                  30

Tyr Leu Val His Trp Tyr Gln Gln Arg Pro Gly Thr Ala Pro Gln Leu
35                  40                  45

Leu Val Ser Gly Asn Asn Thr Arg Pro Ser Gly Val Thr Asp Arg Phe
50                  55                  60

Ser Val Ser Lys Ser Ala Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Thr Tyr Asp Ile Asn
85                  90                  95

Leu Arg Val Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly
100                 105                 110

Ala


<210> SEQ ID NO 17
<211> LENGTH: 125
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 17

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20                  25                  30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35                  40                  45
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Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Leu
50                  55                  60

Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85                  90                  95

Ala Arg Val Pro Gly Val Ser Gly Ser Tyr Pro Asp Tyr Tyr Tyr Met
100                 105                 110

Asp Val Trp Gly Lys Gly Thr Leu Val Thr Val Ser Ser
115                 120                 125


<210> SEQ ID NO 18
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 18

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Ile Gly
1               5                   10                  15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Gly Ile Tyr His Trp
20                  25                  30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35                  40                  45

Tyr Lys Ala Ser Ser Leu Ala Ser Gly Ala Pro Ser Arg Phe Ser Gly
50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Asn Tyr Pro Leu
85                  90                  95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala
100                 105


<210> SEQ ID NO 19
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 19

Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Arg Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Asp Tyr
20                  25                  30

Tyr Met Thr Trp Ile Arg Gln Ile Pro Gly Lys Gly Leu Glu Trp Val
35                  40                  45

Ala Val Ile Trp Asn Asp Gly Ser Asp Arg Tyr Tyr Ala Asp Ser Val
50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Phe
65                  70                  75                  80

Leu Gln Met Ser Ser Leu Arg Asp Glu Asp Thr Ala Leu Tyr Tyr Cys
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85 90 95

Val Arg Gly Gly Pro Thr Ala Ser Ser Gly Phe Asp Tyr Trp Gly Arg
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 20
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolypeptide"

<400> SEQUENCE: 20

Ser Ser Glu Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Leu Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg
85 90 95

Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 21
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolypeptide"

<400> SEQUENCE: 21

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Phe Gly Tyr Asn Phe Arg Ser Ala
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Val Ile Tyr Pro Gly Asp Ser Asp Val Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Thr Arg Pro Val Gly Gln Trp Val Asp Ser Asp Tyr Trp Gly Lys Gly
100 105 110

Thr Leu Val Thr Val Ser Ser
115

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<210> SEQ ID NO 22
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 22

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Thr Asn
20 25 30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Thr Ser Asn Gln Arg Pro Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Ala Ser Asn Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Lys Leu
85 90 95

Ser Gly Ala Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 23
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 23

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Trp Arg Pro Leu Leu Asp Tyr His Phe Asp Gln Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 24
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 24

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Thr Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Ser
20 25 30

Val Val Asn Trp Tyr Gln Gln Phe Pro Gly Thr Ala Pro Lys Val Leu
35 40 45

Val Tyr Ser Asn Thr Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Leu Ala Trp Asp Ala Ser Leu
85 90 95

Asn Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 25
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 25

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Tyr Ser Gly Tyr Asp Asp Pro Asp Ser Trp Gly Arg Gly
100 105 110

Thr Thr Val Thr Val Ser Ser
115

<210> SEQ ID NO 26
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 26

His Val Ile Leu Thr Gln Pro Pro Ser Thr Ser Gly Thr Pro Gly Gln

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1               5                   10                  15

Thr Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser His
20                  25                  30

Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35                  40                  45

Ile Tyr Arg Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65                  70                  75                  80

Ser Glu Asp Glu Thr Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85                  90                  95

Ser Gly Arg Val Phe Gly Thr Gly Thr Lys Leu Thr Val Leu Gly Ala
100                 105                 110


<210> SEQ ID NO 27
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 27

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser
1               5                   10                  15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Ile Ser Asn Tyr
20                  25                  30

Ala Ile Ser Trp Val Arg Leu Ala Pro Gly Gln Gly Leu Glu Trp Met
35                  40                  45

Gly Ser Ile Val Pro Leu His Gly Thr Thr Asn Phe Ala Gln Lys Phe
50                  55                  60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ser Tyr
65                  70                  75                  80

Met Glu Val Asn Val Leu Thr Tyr Glu Asp Thr Ala Met Tyr Tyr Cys
85                  90                  95

Ala Ser Leu Asn Trp Gly Tyr Trp Gly Arg Gly Thr Leu Val Thr Val
100                 105                 110

Ser Ser


<210> SEQ ID NO 28
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 28

Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Glu Ser Pro Gly Lys
1               5                   10                  15

Thr Val Thr Ile Ser Cys Thr Gly Ser Ser Gly Ser Ile Ala Ser Asn
20                  25                  30

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Asp Ser Ala Pro Thr Thr Val
35                  40                  45
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Ile Tyr Glu Asp Asn Arg Arg Ser Ser Gly Val Pro Asp Arg Phe Ser
50                  55                  60

Gly Ser Ile Asp Ser Asn Ser Ala Ser Leu Ser Ile Ser Gly Leu Lys
65                  70                  75                  80

Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser Gly
85                  90                  95

His Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100                 105                 110


<210> SEQ ID NO 29
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 29

Glu Val Gln Leu Val Glu Ser Gly Glu Gly Leu Val Lys Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr Phe Arg Ser Tyr
20                  25                  30

Ser Leu Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Val
35                  40                  45

Ser Ser Ile Ser Ser Thr Ser Thr Tyr Ile Tyr Tyr Ala Asp Ser Val
50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ala Lys Asn Thr Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Ala Tyr Tyr Cys
85                  90                  95

Val Arg Leu Gly Ser Gly Gly Gly Tyr Phe Pro Asp Tyr Trp Gly Arg
100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
115                 120


<210> SEQ ID NO 30
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 30

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1               5                   10                  15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35                  40                  45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
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85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 31
<211> LENGTH: 114
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolypeptide"

<400> SEQUENCE: 31

Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Thr Tyr
20 25 30

Ala Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ser Ile Ser Gly Asp Gly Gly Arg Ile Leu Asp Ala Asp Ser Ala
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Gly Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

Ala Arg Ala Asp Gly Asn Tyr Trp Gly Arg Gly Thr Met Val Thr Val
100 105 110

Ser Ser

<210> SEQ ID NO 32
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolypeptide"

<400> SEQUENCE: 32

Gln Ser Val Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg
85 90 95

Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 33
<211> LENGTH: 121

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 33

Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Asp Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Arg Ser Tyr Gly His Pro Tyr Tyr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 34
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 34

Gln Ser Val Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg
85 90 95

Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 35
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

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<400> SEQUENCE: 35

Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Gly Ile Phe Tyr Asp Gly Gly Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Gly Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> SEQ ID NO 36
<211> LENGTH: 113
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 36

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Arg Ser Ser Asn Ile Gly Ala Gly
20 25 30

His Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
35 40 45

Leu Ile Tyr Gly Asp Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
85 90 95

Leu Arg Gly Ser Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly
100 105 110

Ala

<210> SEQ ID NO 37
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 37

Lys Val Gln Leu Val Gln Ser Gly Thr Glu Val Lys Lys Pro Gly Glu
1 5 10 15

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Ser Leu Lys Ile Ser Cys Gln Gly Ser Gly Tyr Arg Phe Ser Ser Asp
20                  25                  30

Trp Ile Ala Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35                  40                  45

Gly Ile Val Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50                  55                  60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65                  70                  75                  80

Leu Gln Trp Ser Gly Leu Lys Ala Ser Asp Thr Ala Lys Tyr Tyr Cys
85                  90                  95

Ala Arg Val Gln Gln Ala Val Gly Ala Lys Gly Tyr Ala Met Asp Val
100                 105                 110

Trp Gly Lys Gly Thr Leu Val Thr Val Ser Ser
115                 120


<210> SEQ ID NO 38
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 38

Gln Thr Val Val Ile Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1               5                   10                  15

Thr Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser
20                  25                  30

Tyr Tyr Pro Ser Trp Tyr Arg Gln Thr Pro Gly Gln Ala Pro His Thr
35                  40                  45

Leu Ile His Asn Thr Lys Ile Arg Ser Ser Gly Val Pro Asp Arg Phe
50                  55                  60

Ser Gly Ser Ile Leu Gly Asn Asn Ala Ala Leu Thr Ile Thr Gly Ala
65                  70                  75                  80

Gln Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Leu Leu Tyr Met Gly Ser
85                  90                  95

Gly Ile Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100                 105                 110


<210> SEQ ID NO 39
<211> LENGTH: 122
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 39

Gln Val Gln Leu Gln Glu Ser Gly Ala Gly Leu Val Lys Pro Ser Gly
1               5                   10                  15

Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Gly
20                  25                  30

Asn Trp Trp Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
35                  40                  45

Ile Gly Glu Ile Ser His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu
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50                  55                  60

Lys Ser Arg Val Thr Ile Ser Val Asp Lys Ser Lys Asn Gln Phe Ser
65                  70                  75                  80

Leu Asn Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85                  90                  95

Ala Arg Val Arg Gly Thr Val Gly Asp Thr Arg Gly Pro Asp Tyr Trp
100                 105                 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115                 120


<210> SEQ ID NO 40
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 40

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1               5                   10                  15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35                  40                  45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
85                  90                  95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100                 105                 110


<210> SEQ ID NO 41
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 41

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1               5                   10                  15

Ser Val Arg Val Ser Cys Lys Gly Ser Gly Asn Thr Phe Thr Gly His
20                  25                  30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Leu
35                  40                  45

Gly Trp Ile Asp Pro Asn Thr Gly Asp Ile Gln Tyr Ser Glu Asn Phe
50                  55                  60

Lys Gly Ser Val Thr Leu Thr Arg Asp Pro Ser Ile Asn Ser Val Phe
65                  70                  75                  80

Met Asp Leu Ile Arg Leu Thr Ser Asp Asp Thr Ala Met Tyr Tyr Cys
85                  90                  95
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Ala Arg Glu Gly Ala Gly Leu Ala Asn Tyr Tyr Tyr Tyr Gly Leu Asp
100 105 110

Val Trp Gly Arg Gly Thr Met Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 42
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 42

Gln Thr Val Val Leu Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Asn Phe Gly Ser Val Ser Thr Ala
20 25 30

Tyr Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
35 40 45

Leu Ile Tyr Gly Thr Asn Ile Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Val Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Thr Glu Asp Glu Ser Asp Tyr Tyr Cys Ala Leu Tyr Met Gly Ser
85 90 95

Gly Met Leu Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 43
<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 43

Glu Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Ile Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Thr Gly Glu Tyr Ser Gly Tyr Asp Thr Ser Gly Tyr Ser Asn
100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120

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<210> SEQ ID NO 44
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 44

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Thr Val Asn Trp Tyr Gln Arg Leu Pro Gly Ala Ala Pro Gln Leu Leu
35 40 45

Ile Tyr Asn Asn Asp Gln Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Gly Ser Leu Val Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Trp Asp Asp Ser Leu
85 90 95

Asn Gly Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly
100 105 110

<210> SEQ ID NO 45
<211> LENGTH: 121
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 45

Gly Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Asp Thr Ser Gly Trp Tyr Gly Asp Gly Met Asp Val Trp Gly
100 105 110

Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 46
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 46

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Ile Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Gly Ile Tyr His Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Ser Leu Ala Ser Gly Ala Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Asn Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala
100 105

<210> SEQ ID NO 47
<211> LENGTH: 124
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 47

Gln Met Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Ile Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Gly Val Tyr Tyr Cys
85 90 95

Ser Lys Asp Arg Tyr Ser Ser Gly Trp Tyr Ser Ser Asp Ala Phe Asp
100 105 110

Ile Trp Gly Arg Gly Thr Met Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 48
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 48

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

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Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys His Ser Arg Asp Ser Ser Gly Asn His
85 90 95

Val Leu Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 49
<211> LENGTH: 128
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 49

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr Phe Thr Asn His
20 25 30

Trp Ile Ala Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Glu Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly His Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Thr Leu Lys Asp Ser Asp Ser Ala Met Tyr Phe Cys
85 90 95

Val Arg Gln Ala Arg Gly Trp Asp Asp Gly Arg Ala Gly Tyr Tyr Tyr
100 105 110

Ser Gly Met Asp Ala Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 50
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 50

Gln Ala Val Val Leu Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Arg Ser Gly Ser Val Ser Thr Ser
20 25 30

His Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
35 40 45

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Leu Ile Tyr Ser Thr Asn Thr Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Leu Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Asp Asp Glu Ser Asn Tyr Tyr Cys Met Leu Tyr Met Gly Ser
85 90 95

Gly Met Tyr Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 51
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 51

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Val Ser Gly Ser His Phe Pro Phe Phe Asp Ser Trp Gly Gln
100 105 110

Gly Thr Met Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 52
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 52

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asp Lys Ile Gly His Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Leu Val Tyr
35 40 45

Asp Asp Arg Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Ala Tyr His Cys Gln Val Trp Asp Arg Ser Ser Asp Pro

-continued

85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 53
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 53

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Gln Ala Ser Gly Tyr Thr Phe Ser Gly His
20 25 30

Tyr Met His Leu Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile His Pro Thr Ser Gly Gly Thr Thr Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Arg Val Val Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Thr Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Met Ser Gln Asn Tyr Asp Ala Phe Asp Ile Trp Gly Gln Gly
100 105 110

Thr Met Val Thr Val Ser Ser
115

<210> SEQ ID NO 54
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 54

Gln Ala Val Leu Thr Gln Pro Ser Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
20 25 30

Tyr Asp Val Asn Trp Tyr Gln Gln Phe Pro Gly Thr Ala Pro Lys Ile
35 40 45

Ile Val Tyr Gly Asp Arg Pro Ser Gly Ala Pro Asp Arg Phe Ser Gly
50 55 60

Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Arg Ala
65 70 75 80

Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Trp Asp Ser Arg Leu Ser
85 90 95

Ser Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 55

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<211> LENGTH: 123
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 55

Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Val Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Gly Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ser Val Arg Asn Asp Gly Ser Asn Thr Tyr Tyr Thr Asp Ser Val
50 55 60

Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Thr Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys Ser Arg Arg Val Met Tyr Gly Thr Ser Tyr Tyr Phe Asp Tyr
100 105 110

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 56
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 56

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 57
<211> LENGTH: 126
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

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<400> SEQUENCE: 57

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Leu Gly Ile Asp Pro Leu Trp Ser Gly Tyr Tyr Thr Pro
100 105 110

Leu Asp Tyr Trp Gly Arg Gly Thr Met Val Thr Val Ser Ser
115 120 125

<210> SEQ ID NO 58
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 58

His Val Ile Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Ser Val Ser Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Met Tyr Thr Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Ala Ser Leu
85 90 95

Asn Thr Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 59
<211> LENGTH: 116
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 59

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr

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20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Gly Gly Ser Gly Ser Asp Tyr Trp Gly Gln Gly Thr Met Val
100 105 110

Thr Val Ser Ser
115

<210> SEQ ID NO 60
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 60

Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Gly Ser Pro Gly Lys
1 5 10 15

Thr Val Thr Ile Ser Cys Thr Arg Ser Ser Gly Tyr Ile Asp Ser Lys
20 25 30

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Gly Ser Ala Pro Thr Thr Val
35 40 45

Ile Tyr Glu Asp Asn Arg Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Ile Asp Ser Asn Ser Ala Ser Leu Thr Ile Ser Gly Leu Glu
65 70 75 80

Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Asp Thr Asn
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 61
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 61

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Glu Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Asp Phe Ser Asn Tyr
20 25 30

Gly Phe Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ser Tyr Asn Gly Tyr Thr Asn Tyr Ala Gln Arg Leu
50 55 60

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Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr
65                  70                  75                  80

Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85                  90                  95

Ala Arg Asp Arg Gly Leu Gly Asn Trp Tyr Phe Asp Leu Trp Gly Gln
100                 105                 110

Gly Thr Leu Val Thr Val Ser Ser
115                 120


<210> SEQ ID NO 62
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 62

Gln Ser Val Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1               5                   10                  15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20                  25                  30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35                  40                  45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg
85                  90                  95

Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100                 105                 110


<210> SEQ ID NO 63
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 63

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1               5                   10                  15

Thr Ala Arg Met Thr Cys Gly Gly Asn Asn Ile Glu Ser Lys Thr Val
20                  25                  30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35                  40                  45

Asn Asp Asn Val Arg Pro Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser
50                  55                  60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Asn Arg Val Glu Ala Gly
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp Ser Ser Arg Asp Gln
85                  90                  95
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Gly Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> SEQ ID NO 64
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 64

Gln Ala Val Leu Thr Gln Pro Ser Ser Val Ser Ala Ala Pro Gly Gln
1 5 10 15

Glu Val Ser Ile Ser Cys Ser Gly Ala Arg Ser Asn Val Gly Gly Asn
20 25 30

Tyr Val Ser Trp Tyr Gln His Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Met Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Val Gln
65 70 75 80

Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Ser Ser Leu
85 90 95

Ser Ala Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 65
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 65

Gln Val Gln Leu Val Gln Ser Gly Ser Glu Val Arg Arg Pro Gly Ser
1 5 10 15

Ser Val Arg Ile Ser Cys Thr Ala Ser Gly Asp Thr Ser Ser Ser Phe
20 25 30

Thr Val Asn Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Thr Pro Met Phe Gly Thr Ala Asn Tyr Ala Gln Val Phe
50 55 60

Glu Asp Arg Val Thr Ile Ile Ala Asp Glu Met Glu Leu Ser Gly Leu
65 70 75 80

Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Thr Gly Pro Ser Asp
85 90 95

Tyr Val Trp Gly Ser Tyr Arg Phe Leu Asp Asn Trp Gly Arg Gly Thr
100 105 110

Leu Val Thr Val Ser Ser
115

<210> SEQ ID NO 66
<211> LENGTH: 110
<212> TYPE: PRT

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 66

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln
1 5 10 15

Lys Val Thr Ile Ser Cys Ser Gly Gly Arg Ser Ser Ile Gly Asn Asn
20 25 30

Tyr Val Ser Trp Tyr Gln His Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asp Asn Asn Gln Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Trp Asp Ser Ser Leu
85 90 95

Ser Ala Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
100 105 110

<210> SEQ ID NO 67
<211> LENGTH: 119
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 67

Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile Phe Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Ser Ala Lys Asn Ser Val Ser
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Ser Tyr Tyr Ser Tyr Tyr Tyr Gly Met Asp Ala Trp Gly Gln Gly
100 105 110

Thr Met Val Thr Val Ser Ser
115

<210> SEQ ID NO 68
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 68

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Ser Tyr Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20                  25                  30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35                  40                  45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Tyr Ser Leu
85                  90                  95

Ser Gly Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
100                 105                 110


<210> SEQ ID NO 69
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 69

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20                  25                  30

Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35                  40                  45

Ile Tyr Arg Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85                  90                  95

Ser Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100                 105                 110


<210> SEQ ID NO 70
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 70

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln
1               5                   10                  15

Lys Val Thr Ile Ser Cys Ser Gly Ser Thr Ser Asn Ile Gly Asn Asn
20                  25                  30

Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met
35                  40                  45
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Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50                  55                  60

Gly Ser Lys Ser Gly Asn Ser Ala Ser Leu Asp Ile Ser Gly Leu Gln
65                  70                  75                  80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85                  90                  95

Ser Glu Phe Leu Phe Gly Thr Arg Thr Lys Leu Thr Val Leu
100                 105                 110


<210> SEQ ID NO 71
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 71

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1               5                   10                  15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Ala Tyr
20                  25                  30

Asp Phe Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35                  40                  45

Met Ile Tyr Glu Val Asn Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50                  55                  60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser
85                  90                  95

Lys Asn Leu Leu Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100                 105                 110


<210> SEQ ID NO 72
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 72

Gln Ala Val Leu Thr Gln Pro Ser Ala Val Ser Gly Ala Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asn Ile Gly Thr Asn
20                  25                  30

Tyr Leu Val His Trp Tyr Gln Gln Arg Pro Gly Thr Ala Pro Gln Leu
35                  40                  45

Leu Val Ser Gly Asn Asn Thr Arg Pro Ser Gly Val Thr Asp Arg Phe
50                  55                  60

Ser Val Ser Lys Ser Ala Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65                  70                  75                  80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Thr Tyr Asp Ile Asn
85                  90                  95

Leu Arg Val Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
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100 105 110

<210> SEQ ID NO 73
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolypeptide"

<400> SEQUENCE: 73

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Ile Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Gly Ile Tyr His Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Ser Leu Ala Ser Gly Ala Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Asn Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> SEQ ID NO 74
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolypeptide"

<400> SEQUENCE: 74

Ser Ser Glu Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Leu Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg
85 90 95

Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 75
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:

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Syntheticpolypeptide"

<400> SEQUENCE: 75

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Thr Asn
20 25 30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Thr Ser Asn Gln Arg Pro Ser Gly Val Pro Ala Arg Phe Ser
50 55 60

Ala Ser Asn Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Lys Leu
85 90 95

Ser Gly Ala Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 76
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 76

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Thr Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Ser
20 25 30

Val Val Asn Trp Tyr Gln Gln Phe Pro Gly Thr Ala Pro Lys Val Leu
35 40 45

Val Tyr Ser Asn Thr Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Leu Ala Trp Asp Ala Ser Leu
85 90 95

Asn Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 77
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 77

His Val Ile Leu Thr Gln Pro Pro Ser Thr Ser Gly Thr Pro Gly Gln
1 5 10 15

Thr Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser His
20 25 30

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Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35                  40                  45

Ile Tyr Arg Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50                  55                  60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65                  70                  75                  80

Ser Glu Asp Glu Thr Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
85                  90                  95

Ser Gly Arg Val Phe Gly Thr Gly Thr Lys Leu Thr Val Leu
100                 105                 110


<210> SEQ ID NO 78
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 78

Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Glu Ser Pro Gly Lys
1               5                   10                  15

Thr Val Thr Ile Ser Cys Thr Gly Ser Ser Gly Ser Ile Ala Ser Asn
20                  25                  30

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Asp Ser Ala Pro Thr Thr Val
35                  40                  45

Ile Tyr Glu Asp Asn Arg Arg Ser Ser Gly Val Pro Asp Arg Phe Ser
50                  55                  60

Gly Ser Ile Asp Ser Asn Ser Ala Ser Leu Ser Ile Ser Gly Leu Lys
65                  70                  75                  80

Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser Gly
85                  90                  95

His Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100                 105


<210> SEQ ID NO 79
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 79

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1               5                   10                  15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35                  40                  45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
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85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> SEQ ID NO 80
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolypeptide"

<400> SEQUENCE: 80

Gln Ser Val Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg
85 90 95

Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 81
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolypeptide"

<400> SEQUENCE: 81

Gln Ser Val Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg
85 90 95

Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 82
<211> LENGTH: 111
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 82

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Arg Ser Ser Asn Ile Gly Ala Gly
20 25 30

His Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
35 40 45

Leu Ile Tyr Gly Asp Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
85 90 95

Leu Arg Gly Ser Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
100 105 110

<210> SEQ ID NO 83
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 83

Gln Thr Val Val Ile Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser
20 25 30

Tyr Tyr Pro Ser Trp Tyr Arg Gln Thr Pro Gly Gln Ala Pro His Thr
35 40 45

Leu Ile His Asn Thr Lys Ile Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Leu Gly Asn Asn Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Leu Leu Tyr Met Gly Ser
85 90 95

Gly Ile Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 84
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 84

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

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Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> SEQ ID NO 85
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 85

Gln Thr Val Val Leu Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Asn Phe Gly Ser Val Ser Thr Ala
20 25 30

Tyr Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
35 40 45

Leu Ile Tyr Gly Thr Asn Ile Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Val Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Thr Glu Asp Glu Ser Asp Tyr Tyr Cys Ala Leu Tyr Met Gly Ser
85 90 95

Gly Met Leu Phe Gly Gly Gly Thr Lys Val Thr Val Leu
100 105

<210> SEQ ID NO 86
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 86

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Thr Val Asn Trp Tyr Gln Arg Leu Pro Gly Ala Ala Pro Gln Leu Leu
35 40 45

Ile Tyr Asn Asn Asp Gln Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Gly Ser Leu Val Ile Ser Gly Leu Gln

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65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Trp Asp Asp Ser Leu
85 90 95

Asn Gly Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

<210> SEQ ID NO 87
<211> LENGTH: 107
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 87

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Ile Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Gly Ile Tyr His Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Ser Leu Ala Ser Gly Ala Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Asn Tyr Pro Leu
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105

<210> SEQ ID NO 88
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 88

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys His Ser Arg Asp Ser Ser Gly Asn His
85 90 95

Val Leu Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105

<210> SEQ ID NO 89

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<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 89

Gln Ala Val Val Leu Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Arg Ser Gly Ser Val Ser Thr Ser
20 25 30

His Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
35 40 45

Leu Ile Tyr Ser Thr Asn Thr Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Leu Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Asp Asp Glu Ser Asn Tyr Tyr Cys Met Leu Tyr Met Gly Ser
85 90 95

Gly Met Tyr Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
100 105 110

<210> SEQ ID NO 90
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 90

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asp Lys Ile Gly His Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Leu Val Tyr
35 40 45

Asp Asp Arg Lys Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Ala Tyr His Cys Gln Val Trp Asp Arg Ser Ser Asp Pro
85 90 95

Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100 105

<210> SEQ ID NO 91
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 91

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Gln Ala Val Leu Thr Gln Pro Ser Ser Val Ser Gly Ala Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
20                  25                  30

Tyr Asp Val Asn Trp Tyr Gln Gln Phe Pro Gly Thr Ala Pro Lys Ile
35                  40                  45

Ile Val Tyr Gly Asp Arg Pro Ser Gly Ala Pro Asp Arg Phe Ser Gly
50                  55                  60

Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Arg Ala
65                  70                  75                  80

Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Trp Asp Ser Arg Leu Ser
85                  90                  95

Ser Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu
100                 105


<210> SEQ ID NO 92
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 92

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1               5                   10                  15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20                  25                  30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35                  40                  45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50                  55                  60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65                  70                  75                  80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His
85                  90                  95

Val Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100                 105


<210> SEQ ID NO 93
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 93

His Val Ile Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1               5                   10                  15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20                  25                  30

Ser Val Ser Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35                  40                  45

Met Tyr Thr Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
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50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Ala Ser Leu
85 90 95

Asn Thr Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
100 105 110

<210> SEQ ID NO 94
<211> LENGTH: 108
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 94

Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Gly Ser Pro Gly Lys
1 5 10 15

Thr Val Thr Ile Ser Cys Thr Arg Ser Ser Gly Tyr Ile Asp Ser Lys
20 25 30

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Gly Ser Ala Pro Thr Thr Val
35 40 45

Ile Tyr Glu Asp Asn Arg Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Ile Asp Ser Asn Ser Ala Ser Leu Thr Ile Ser Gly Leu Glu
65 70 75 80

Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Asp Thr Asn
85 90 95

Val Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
100 105

<210> SEQ ID NO 95
<211> LENGTH: 110
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 95

Gln Ser Val Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg
85 90 95

Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
100 105 110

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<210> SEQ ID NO 96
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 96

gaggtccagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggata caccttcacc ggctactata tgcactgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat 180

gcacagaagt ttcagggctg ggtcaccatg accagggaca cgtccatcag cacagcctac 240

atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagagattct 300

actatggccc caggtgcttt tgatatctgg ggccgaggca ccctggtcac cgtctcgagt 360

<210> SEQ ID NO 97
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 97

cagtctgtgc tgactcagcc accctcggtg tcagtggccc caggacagac ggccaggatg 60

acctgtgggg gaaacaacat tgaaagtaaa actgtgcatt ggtaccagca gaagccgggc 120

caggcccctg tgctggtcgt ctacaatgat aacgtccggc cctcagggat ccctgcgcga 180

ttctctggct ccaactccgg caacacggcc accctgacca tcaacagggt cgaagccggg 240

gatgaggccg actattattg tcaggtgtgg gactccagta gagatcaagg ggtattcggc 300

ggagggacca agctgaccgt c 321

<210> SEQ ID NO 98
<211> LENGTH: 320
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 98

ggaggcctgg gtcctcggtg agggtctcct gcacggcttc tggagacacc tccagcagct 60

ttaccgtcaa ctggctgcga caggcccctg gacaaggtct tgagtggatg ggagggatca 120

cccctatgtt tggcactgca aactacgcac agatgttcga ggacagagtc acgataaccg 180

cggacgaaat ggaactgagt ggcctgacat ctgaggacac ggccgtgtat ttttgtgcga 240

caggcccctc cgattacgtt tgggggagtt atcgtttcct tgacacctgg gggcgggggga 300

ccacggtcac cgtctcgagt 320

<210> SEQ ID NO 99
<211> LENGTH: 330

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 99

caggctgtgc tgactcagcc gtcctcagtg tctgcggccc caggacagga ggtctccatc 60

tcctgctctg gagccagatc caacgttggg ggtaattatg tttcctggta ccaacacctc 120

ccaggaacag cccccaaact cctcatttat gacaataata agcgaccctc agggatgcct 180

gaccgattct ctggctccaa gtctggcacg tcagccaccc tgggcatcac cggagtccag 240

actgaggacg aggccgatta ttactgcgca acatgggata gcagcctgag cgctgtggtc 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 100
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 100

caggtgcagc tggtgcagtc tgggtctgag gtgaggaggc ctgggtcctc ggtgaggatc 60

tcctgcacgg cttctggaga cacctccagc agctttaccg tcaactgggt gcgacaggcc 120

cctggacaag gtcttgagtg gatgggaggg atcaccccta tgtttggcac tgcaaactac 180

gcacaggtgt tcgaggacag agtcacaata atcgcggacg agatggaact gagtggcctg 240

acatctgagg acacggccgt gtatttctgt gcgacaggcc cctccgatta cgtttggggg 300

agttatcgtt tccttgacaa ctggggcagg ggcaccctgg tcaccgtctc gagt 354

<210> SEQ ID NO 101
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 101

cagtctgtgc tgactcagcc accctcagtg tctgcggccc cagggcagaa ggtcaccatc 60

tcctgctctg gaggcaggtc cagcattggg aataattatg tgtcctggta tcaacacctc 120

ccaggaacag cccccaaact cctcatctat gacaataatc agcgaccctc agggattcct 180

gaccgattct ctggctccaa gtctggcacg tcagccaccc tgggcatcac cggactccag 240

actggggacg aggccgatta ttactgcgga acatgggata gcagcctgag tgctgtggtg 300

tttggcggag ggaccaaggt caccgtccta 330

<210> SEQ ID NO 102
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

<400> SEQUENCE: 102

gaggtgcagc tggtggagac tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatggca tgaactgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtttcatac attagtagtt ctggtaatac catattctac 180

gcagactctg tgaagggccg attcaccatc tccagagaca gtgccaagaa ttcagtgtct 240

ctgcagatga acagcctgag agacgaggac acggctgtgt attactgtgc ttcctactac 300

tcctactact acggtatgga cgcctggggc caggggacaa tggtcaccgt ctcgagttcg 360

agt 363

<210> SEQ ID NO 103
<211> LENGTH: 300
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

<400> SEQUENCE: 103

tctgggaccc ccgggcagag ggtcaccatc tcttgttctg gaagcagctc caacatcgga 60

agtaatactg taaactggta ccagcagctc ccaggaacgg cccccaaact cctcatctat 120

agtaataatc agcggccctc aggggtccct gaccgattct ctggctccaa gtctggcacc 180

tcagcctccc tggccatcag tgggctgcgg tccgaggatg aggctgatta ttactgtgca 240

gcatgggatt acagcctgag tggttgggtg ttcggcggag ggaccaaggt caccgtccta 300

<210> SEQ ID NO 104
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

<400> SEQUENCE: 104

gaagtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctgggta cagcttcacc gccttctata ttcactgggt gcgacaggcc 120

cctggacaag gccttgagta tttgggatgg atcgacccta atactggtgc cacaaaatat 180

gcacagcgct ttcagggcag ggtcatcatg acctgggaca cgtccatcac cacagccacc 240

atggaactga gcaggctgac gtctgacgac tcggccgtct actactgtgt gagagatttg 300

cgggagtggg gctacgaatt gtccgttgag tattggggca gaggaaccct ggtcaccgtc 360

tcgagt 366

<210> SEQ ID NO 105
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

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<400> SEQUENCE: 105

cagtctgtgc tgactcagcc accctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcgga agtaattatg tatactggta ccagcagctc 120

ccaggaacgg cccccaaact cctcatctat aggaataatc agcggccctc aggggtccct 180

gaccgattct ctggctccaa gtctggcacc tcagcctccc tggccatcag tgggctccgg 240

tccgaggatg aggctgatta ttactgtgca gcatgggatg acagcctgag tggttgggtg 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 106
<211> LENGTH: 345
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 106

gaggtgcagc tggtggagac tgggggaggc gtggtccagc ctgggggtc cctgagcctc 60

tcctgtgcag cgtctggatt caccttcagt agctatggca tgcagtgggt ccgccaggct 120

ccaggcaagg ggctggagtg ggtggcgttt atacggtacg atggaagtag tgaatactat 180

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgg aagaacgctg 300

gagtctagtt tgtggggcaa gggaaccctg gtcaccgtct cgagt 345

<210> SEQ ID NO 107
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 107

cagtctgtgt tgacgcagcc gccctcagtg tctgcggccc caggacagaa ggtcaccatt 60

tcctgctctg gaagcacctc caacattggg aataattatg tctcctggta ccaacagcac 120

ccaggcaaag cccccaaact catgatttat gatgtcagta agcggccctc aggggtccct 180

gaccgattct ctggctccaa gtctggcaac tcagcctccc tggacatcag tgggctccag 240

tctgaggatg aggctgatta ttactgtgca gcatgggatg acagcctgag tgaatttctc 300

ttcggaacta ggaccaagct gaccgtccta 330

<210> SEQ ID NO 108
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 108

caggtgcagc tgcaggagtc gggtccagga ctggtgaagc cctcgcagac cttgtcactc 60

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acctgtggca tctccgggga cagtgtctct agcaacagtg ctgcttggaa ctggatcagg 120

cagtccccaa cgagaggcct tgagtggctg ggaaggacat attacaggtc cagttggtat 180

cataactatg caccttctat gaacagtcga ttaaccatca tcgcagacac atccaaaaac 240

cagttctctt tgcaactgaa ctctgtgact cccgaggaca cggctgtata ttactgtgca 300

agcgggtggg cctttgatgt ctggggcagg ggaaccctgg tcaccgtctc gagt 354

<210> SEQ ID NO 109
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 109

cagtctgtgc tgactcagcc accctccgcg tccgggtctc ctggacagtc agtcaccatc 60

tcctgcactg gaaccagcag tgacgttggt gcttatgact ttgtctcctg gtaccaacag 120

caccctggca aagcccccaa actcatgatt tatgaggtca ataagcggcc ctcaggggtc 180

cctgatcgct tctctggctc caagtctggc aacacggcct ccctgaccgt ctctgggctc 240

caggctgagg atgaggctga ttattactgc agctcatatg caggcagcaa gaatttgctt 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 110
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 110

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagacagtcg 300

ggcgcggact ggtacttcga tctctggggc cgaggcaccc tggtcaccgt ctcgagt 357

<210> SEQ ID NO 111
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 111

caggctgtgc tgactcagcc gtccgcagtt tctggggccc cagggcagag ggtcaccatc 60

tcctgcactg ggaccagctc caacatcggg acaaactatc ttgtacactg gtatcagcaa 120

cgtccaggaa cagcccccca actcctcgtc tctggtaaca acactcgacc ctctggggtc 180

-continued

actgaccggt tctctgtctc caagtctgcc acttcagcct ccctggccat cactgggctc 240

caggctgagg atgaggctga ttattactgc cagacctatg acatcaactt gagggtttgg 300

gtgttcggcg gagggaccaa ggtcaccgtc cta 333

<210> SEQ ID NO 112
<211> LENGTH: 375
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 112

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 120

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 180

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagtcccg 300

ggcgtaagtg ggagctatcc agactactac tacatggacg tctggggcaa gggaaccctg 360

gtcaccgtct cctca 375

<210> SEQ ID NO 113
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 113

gacatccaga tgacccagtc tccttccacc ctgtctgcat ctattggaga cagagtcacc 60

atcacctgcc gggccagtga gggtatttat cactggttgg cctggtatca gcagaagcca 120

gggaaagctc ctaaactcct gatctataag gcctctagtt tagccagtgg ggccccatca 180

aggttcagcg gcagtggatc tgggacagat ttcactctca ccatcagcag cctgcagcct 240

gatgattttg caacttatta ctgccaacaa tatagtaatt atccgctcac tttcggcgga 300

gggaccaagc tggagatcaa a 321

<210> SEQ ID NO 114
<211> LENGTH: 359
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 114

gaggtgcagc tggtgcagtc tgggggaggc ttggtcaggc ctggagggtc cctgagactc 60

tcctgtgcag cctcgggatt ctccttcagt gactactaca tgacctggat ccgccagatt 120

ccagggaagg ggctggagtg ggtggcagtt atatggaatg atggaagtga tagatactat 180

gcagactccg tgaagggccg attcaccatt tccagagaca attccaagaa cacgctgttt 240

-continued

ctgcaaatga gcagcctgag agacgaggac acggctctat attactgtgt gagaggggga 300

ccaacagctt caagcggatt tgactactgg ggccgaggca ccctggtcac cgtctcgag 359

<210> SEQ ID NO 115
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 115

tcgtctgagc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtacctacaa 120

cacccaggca aagcccccaa actcatgatt tatgagggca gtaagcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgacaat ctctgggctc 240

caggctgagg acgaggctga ttattactgc agctcatata caaccaggag cactcgagtt 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 116
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 116

gaggtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtaagg gttttggata caattttcgc agcgcctgga tcggctgggt gcgccagatg 120

cccggcaaag gcctggagtg gatgggggtc atctatcctg gtgactctga tgtcagatac 180

agtccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag taccgcctac 240

ctgcagtgga gcagcctgaa agcctcggac accgccatgt attattgtac gagacccgta 300

gggcagtggg tggactctga ctattggggc aagggaaccc tggtcaccgt ctcgagt 357

<210> SEQ ID NO 117
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 117

cagtctgtgt tgacgcagcc gccctcagcg tctgggaccc ccggacagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcgga actaatactg tgaactggta ccagcagctt 120

ccaggaacgg cccccaaact cctcatctat actagtaatc agcggccctc aggggtccct 180

gcccgcttct ctgcctccaa ctctggcacc tcagcctccc tggccatcag tgggctccgg 240

tccgaggatg aggctgatta ttattgtgca gcgtgggatg acaagttgag tggtgcggtg 300

ttcggcggag ggaccaagct gaccgtccta 330

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<210> SEQ ID NO 118
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 118

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagatggagg 300

cctcttctag actaccactt tgaccaatgg ggccaaggga caatggtcac cgtctcgagt 360

<210> SEQ ID NO 119
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 119

cagtctgtgc tgactcagcc accctcagcg tctgggaccc ccggacagac ggtaacaatc 60

tcttgttctg gaagcagctc caacatcgga agtagtgttg ttaattggta ccagcagttc 120

ccaggaacgg cccccaaagt cctcgtctat agtaacactc agcggccctc aggggtccct 180

gaccgattct ctggctccag gtctggcacc tcagcctccc tggccatcag tgggctccag 240

tctgaggatg aggctgatta ttactgttta gcatgggatg ccagcctgaa tggttgggtg 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 120
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 120

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagaggatac 300

agtggctacg atgaccctga ctcctggggg agagggacca cggtcaccgt ctcgagt 357

<210> SEQ ID NO 121
<211> LENGTH: 330

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 121

cacgttatac tgactcaacc gccctcaacg tctgggaccc ccgggcagac ggtcaccatc 60

tcttgttctg ggagcagctc caacatcgga agtcattatg tatactggta ccagcagctc 120

ccaggaacgg cccccaaact cctcatctat aggaataatc agcggccctc aggggtccct 180

gaccgattct ctggctccaa gtctggcacc tcagcctccc tggccatcag tgggctccgg 240

tccgaggatg agactgatta ttactgtgca gcatgggatg acagcctgag tggtcgagtc 300

ttcggaactg ggaccaagct gaccgtccta 330

<210> SEQ ID NO 122
<211> LENGTH: 342
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 122

caggtacagc tgcagcagtc aggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 60

tcctgcaagg cttctggagg caccatcagc aactatgcta tcagttgggt gcggctggcc 120

cctggacaag gtcttgagtg gatgggaagt atcgtccctc ttcatgggac aacaaacttc 180

gcacagaaat tccagggcag agtcacgatc accgcggacg agtccacgag cacatcctac 240

atggaggtga acgtcctgac atatgaagac acggcgatgt attattgtgc gtctctcaat 300

tggggctact ggggccgggg caccctggtc accgtctcga gt 342

<210> SEQ ID NO 123
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 123

aattttatgc tgactcagcc ccactctgtg tcggagtctc cggggaagac ggtaaccatc 60

tcctgcaccg gcagtagtgg cagcattgcc agcaactatg tgcagtggta ccagcagcgc 120

ccggacagtg cccccaccac tgtgatctat gaggataatc gaagatcctc tggagtccct 180

gatcggttct ctggctccat cgacagctcc tccaactctg cctccctcag catctctgga 240

ctgaagactg aggacgaggc tgactactac tgtcagtcct atgatagtag cggtcatgtg 300

gtcttcggcg gagggaccaa gctgaccgtc cta 333

<210> SEQ ID NO 124
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

<400> SEQUENCE: 124

gaggtgcagc tggtggagtc tggggaaggc ctggtcaagc ctgggggtc cctgagactc 60

tcctgtacag cctctggatt caccttcagg agttatagct tgaactgggt ccgccaggct 120

ccagggcagg ggctggagtg ggtctcatcc attagtagta ctagtactta catatactac 180

gcagactcgg tgaagggccg attcaccatc tccagagacg acgccaagaa cacactgtat 240

ctgcaaatga acagcctgag agccgaagac acagctgcat attactgtgt tagactggga 300

tctggtgggg gatattttcc tgactactgg ggcaggggca ccctggtcac cgtctcgagt 360

<210> SEQ ID NO 125
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

<400> SEQUENCE: 125

tcgtctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaaccatgt ggtattcggc 300

ggagggacca agctgaccgt ccta 324

<210> SEQ ID NO 126
<211> LENGTH: 342
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

<400> SEQUENCE: 126

caggtgcagc tggtgcagtc tgggggaggc ttggtccagc cgggggggtc cctgagactc 60

tcctgtgcag cctctggatt cacgtttagt acctatgcca tgagttgggc ccgccaggct 120

ccagggaagg ggctggagtg ggtctcaagt attagtggtg atggtggaag aattctcgat 180

gcagactccg cgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acggcctgag agtcgaggac acggcccttt attactgtgc gagagcggac 300

ggtaactact ggggcagggg gacaatggtc accgtctctt ca 342

<210> SEQ ID NO 127
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

<400> SEQUENCE: 127

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cagtctgtgc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcatgatt tatgagggca gtaagcggcc tcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgacaat ctctgggctc 240

caggctgagg acgaggctga ttattactgc agctcatata caaccaggag cactcgagtt 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 128
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 128

caggtgcagc tggtggagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 60

tcctgcaagg cttctggata caccttcacc agttatgata tcaactgggt gcgacaggcc 120

cccggacaaa ggcttgagtg gatgggatgg atcaacgctg gcaatggtaa cacaaaatat 180

tcacagaagt tccagggcag agtcaccatt accagggaca catccgcgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagggagg 300

agctatggcc acccgtacta ctttgactac tggggccagg gaaccctggt caccgtctcg 360

agt 363

<210> SEQ ID NO 129
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 129

cagtctgtgc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcatgatt tatgagggca gtaagcggcc tcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgacaat ctctgggctc 240

caggctgagg acgaggctga ttattactgc agctcatata caaccaggag cactcgagtt 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 130
<211> LENGTH: 354
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 130

gaggtgcagc tggtgcagtc tgggggaggc ctggtcaagc ctgggggggtc cctgagactc 60

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tcctgtgcag cgtctggatt caccttcagt agctatggga tgcactgggt ccgccaggct 120

ccaggcaagg ggctggagtg ggtggcaggt atttttttatg atggaggtaa taaatactat 180

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gagagatagg 300

ggctactact acatggacgt ctggggcaaa gggaccacgg tcaccgtctc ctca 354

<210> SEQ ID NO 131
<211> LENGTH: 333
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 131

cagtctgtgt tgacgcagcc gccctcagtg tctggggccc caggacagag ggtcaccatc 60

tcctgcactg ggagaagctc caacatcggg gcgggtcatg atgtacactg gtaccagcaa 120

cttccaggaa cagccccaa actcctcatc tatggtgaca gcaatcggcc ctcaggggtc 180

cctgaccgat tctctggctc caggtctggc acctcagcct ccctggccat cactgggctc 240

caggctgaag atgaggctga ttattactgc cagtcctatg acagcagcct gaggggttcg 300

gtattcggcg gagggaccaa ggtcaccgtc cta 333

<210> SEQ ID NO 132
<211> LENGTH: 369
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 132

aaggtgcagc tggtgcagtc tgggacagag gtgaaaaagc ccggggagtc tctgaagatc 60

tcctgtcagg gttctggata caggtttagt agtgactgga ttgcctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatggggatt gtctatcctg gtgactctga taccagatat 180

agcccgtcct tccaaggcca agtcaccatc tcagccgaca agtccatcag tactgcctac 240

ctgcagtgga gcggcctgaa ggcctcggac accgccaagt attactgtgc gagagtgcaa 300

caggcagtgg gagctaaagg ttatgctatg gacgtctggg gcaagggaac cctggtcacc 360

gtctcgagt 369

<210> SEQ ID NO 133
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 133

cagactgtgg tgatccagga gccatcgttc tcagtgtccc ctggagggac agtcacactc 60

acttgtggct tgagctctgg ctcagtctct accagttact accccagctg gtaccggcag 120

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accccaggcc aggctccaca cacactcatt cacaacacaa agattcgctc ctctggggtc 180

cctgatcgct tctctggctc catccttggg aacaatgctg ccctcaccat cacgggggcc 240

caggcagatg atgaatctga ttattactgt cttttgtata tgggtagcgg catttacgtg 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 134
<211> LENGTH: 366
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 134

caggtgcagc tgcaggagtc gggcgcagga ctggtgaagc cttcggggac cctgtccctc 60

acctgcgctg tctctggtgg ctccatcagc agtggtaact ggtggagttg ggtccgccag 120

cccccaggga aggggctgga gtggattggg gaaatctctc atagtgggag caccaactac 180

aacccgtccc tcaagagtcg agtcaccata tcagtagaca agtccaagaa ccagttctcc 240

ctgaacctga gttctgtgac cgccgcagac acggccgtgt attactgtgc gagagtaagg 300

ggtacggtgg gggatacacg gggacctgac tactggggcc agggaaccct ggtcaccgtc 360

tcgagt 366

<210> SEQ ID NO 135
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 135

tcgtctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaaccatgt ggtattcggc 300

ggagggacca agctgaccgt ccta 324

<210> SEQ ID NO 136
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 136

gaagtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgagggtc 60

tcctgcaagg gttctggaaa caccttcacc ggccactaca tccactgggt gcgacaggcc 120

cctggacaag gacttgagtg gctgggatgg atcgacccta acactggtga catacagtat 180

-continued

tcagaaaact ttaagggctc ggtcaccttg accagggacc catccatcaa ctcagtcttc 240

atggacctga tcaggctgac atctgacgac acggccatgt attactgtgc gagagaaggt 300

gccgggctcg ccaactacta ttactacggt ctggacgtct ggggccgagg gacaatggtc 360

accgtctcga gt 372

<210> SEQ ID NO 137
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 137

cagactgtgg tgctccagga gccttcgttc tcagtgtccc ctgggggggac agtcacactc 60

acttgtggct tgaactttgg ctcagtctct actgcttact accccagttg gtaccagcag 120

accccaggcc aagctccacg cacgctcatc tacggcacaa atattcgttc ctctggggtc 180

ccggatcgct tctctggctc catcgtaggg aacaaagctg ccctcaccat cacgggggcc 240

cagacagaag atgagtctga ttattattgt gcgctgtata tgggtagtgg catgctcttc 300

ggcggcggga ccaaggtcac cgtccta 327

<210> SEQ ID NO 138
<211> LENGTH: 369
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 138

gaggtgcagc tggtgcagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120

ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtat taaatactat 180

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gcgaactggt 300

gaatatagtg gctacgatac gagtggttac agcaattggg gccaaggcac cctggtcacc 360

gtctcgagt 369

<210> SEQ ID NO 139
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 139

cagtctgtgc tgactcagcc accctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcggg agtaacactg taaactggta ccagcgactc 120

ccaggagcgg ccccccaact cctcatctac aataatgacc agcggccctc agggatccct 180

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gaccgattct ctggctccaa gtctggcacc tcaggctccc tggtcatcag tgggctccag 240

tctgaagatg aggctgatta ctactgtgcg tcatgggatg acagtctgaa tggtcgggtg 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 140
<211> LENGTH: 363
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 140

ggggtgcagc tggtggagtc tgggggaggc ctggtcaagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctataaca tgaactgggt ccgccaggct 120

ccagggaagg gactggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgacgggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagatacc 300

agtggctggt acggggacgg tatggacgtc tggggccggg gaaccctggt caccgtctcg 360

agt 363

<210> SEQ ID NO 141
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 141

gacatccaga tgacccagtc tccttccacc ctgtctgcat ctattggaga cagagtcacc 60

atcacctgcc gggccagtga gggtatttat cactggttgg cctggtatca gcagaagcca 120

gggaaagccc ctaaactcct gatctataag gcctctagtt tagccagtgg ggccccatca 180

aggttcagcg gcagtggatc agggacagat ttcactctca ccatcagcag cctgcagcct 240

gatgattttg caacttatta ctgccaacaa tatagtaatt atccgctcac tttcggcgga 300

gggaccaagc tggagatcaa a 321

<210> SEQ ID NO 142
<211> LENGTH: 372
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 142

cagatgcagc tggtgcagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60

tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 120

ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtat taaatactat 180

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacactgtat 240

-continued

ctacaaatga acagcctgag agccgaggac acgggcgttt attactgttc gaaagatcgc 300

tatagcagtg gctggtacag ctccgatgct tttgatattt ggggccgagg gacaatggtc 360

accgtctcga gt 372

<210> SEQ ID NO 143
<211> LENGTH: 321
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 143

tctgagctga ctcaggaccc tgctgtgtct gtggccttgg gacagacagt caggatcaca 60

tgccaaggag acagcctcag aagctattat gcaagctggt accagcagaa gccaggacag 120

gcccctgtac ttgtcatcta tggtaaaaac aaccggccct cagggatccc agaccgattc 180

tctggctcca gctcaggaaa cacagcttcc ttgaccatca ctggggctca ggcggaagat 240

gaggctgact attactgtca ttcccgggac agcagtggta accatgtgct tttcggcgga 300

gggaccaagc tgaccgtcct a 321

<210> SEQ ID NO 144
<211> LENGTH: 384
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 144

gaggtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggagagtc tctgaagatc 60

tcctgtaagg gctctggata cacctttacc aaccactgga tcgcctgggt gcgccagatg 120

cccgggaaag gcctggagtg gatgggcatc atctatcctg gtgactctga aacgaggtac 180

agcccgtcct tccaaggcca cgtcaccatc tcagccgaca agtccatcag taccgcctat 240

ttgcagtgga gcaccctgaa ggactcggac tccgccatgt acttctgtgt gagacaggcc 300

cgtggctggg acgacggacg ggctggatat tattattccg gtatggacgc ctggggccag 360

ggaaccctgg tcaccgtctc gagt 384

<210> SEQ ID NO 145
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 145

caggctgtgg tgctccagga gccatcgttc tcagtgtccc ctggagggac agtcacactc 60

acctgtggct tgcgctctgg gtcagtctct actagtcact accccagctg gtaccagcag 120

accccaggcc aggctccacg cacgctcatt tacagcacaa acactcgctc ttctggggtc 180

cctgatcgct tctctggctc catccttggg aacaaagctg ccctcaccat cacgggggcc 240

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caggcagatg atgaatctaa ttattactgt atgctataca tgggcagtgg catgtatgtg 300

ttcggcggag ggaccaaggt caccgtccta 330

<210> SEQ ID NO 146
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 146

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagtcagc 300

gggagccact ttccattctt tgactcctgg ggccagggga caatggtcac cgtctcgagt 360

<210> SEQ ID NO 147
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 147

cagtctgtgc tgactcagcc accctcggtg tcagtggccc caggacagac ggccagaatt 60

acctgtgggg gagacaagat tggacataaa agtgtgcatt ggtatcagca gaagccaggc 120

caggcccctg tgttgctcgt ctatgatgat aggaagcggc cctcagggat ccctgagcga 180

ttctctggct ccaactctgg gaacacggcc accctgacca tcagcagggt cgaggccggg 240

gatgaggctg cctatcactg tcaggtgtgg gatagaagta gtgaccctta tgtcttcgga 300

actgggacca aggtcaccgt ccta 324

<210> SEQ ID NO 148
<211> LENGTH: 357
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 148

caggtgcagc tggtgcaatc tggggctgaa gtgaagaagc ctggggcctc agtgaaggtc 60

tcttgtcagg cttctggata caccttcagc gggcactata tgcacttggt gcgacaggcc 120

cctggacaag ggcttgagtg gatggggtgg atccacccta ccagtggtgg cacaacctat 180

gcacagaagt ttcagggccg ggtcgttatg accagggaca cgtccatcag cacagcctac 240

atggaactga gtaggctgac atctgacgac acggccgtgt attactgtgc aagaatgtcc 300

caaaactatg atgcttttga tatctggggc caagggacaa tggtcaccgt ctcgagt 357

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<210> SEQ ID NO 149
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 149

caggctgtgc tgactcagcc gtcctcagtg tctggggccc cagggcagag ggtcaccatc 60

tcctgcactg ggagcagctc caacatcggg gcaggttatg atgtaaactg gtaccaacaa 120

tttccaggaa cagcccccaa aattatcgtc tatggcgatc ggccctcagg ggcccctgac 180

cgattctctg gctccaagtc tggcacctca gcctccctgg caatcactgg actccgggct 240

gaggatgagg ctgattatta ctgccagtcc tgggacagtc gcctgagtag ttatgtcttc 300

ggaactggga ccaaggtcac cgtccta 327

<210> SEQ ID NO 150
<211> LENGTH: 369
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 150

caggtgcagc tgcaggagtc gggggggaggc gtggtccagc ctgggggggtc cctgagactc 60

tcctgtgcag cgtctggatt caccttcagt ggctatggca tgcactgggt ccgccaggct 120

ccaggcaagg ggctggagtg ggtggcatct gtacggaacg atggaagtaa tacatactac 180

acagactccg tgaaggaccg attcaccatc tccagagaca acaccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc caagtcgaga 300

agagtgatgt atggcacctc ctattacttt gactactggg gcagaggcac cctggtcacc 360

gtctcctca 369

<210> SEQ ID NO 151
<211> LENGTH: 324
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 151

tcgtctgagc tgactcagga ccctgctgtg tctgtggcct tgggacagac agtcaggatc 60

acatgccaag gagacagcct cagaagctat tatgcaagct ggtaccagca gaagccagga 120

caggcccctg tacttgtcat ctatggtaaa aacaaccggc cctcagggat cccagaccga 180

ttctctggct ccagctcagg aaacacagct tccttgacca tcactggggc tcaggcggaa 240

gatgaggctg actattactg taactcccgg gacagcagtg gtaaccatgt ggtattcggc 300

ggagggacca agctgaccgt ccta 324

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<210> SEQ ID NO 152
<211> LENGTH: 378
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 152

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatctg 300

ggaatagacc ccctttggag tggttattac acacccctttg actattgggg ccgagggaca 360

atggtcaccg tctcgagt 378

<210> SEQ ID NO 153
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 153

cacgttatac tgactcaacc gccctcagcg tctgggaccc ccgggcagag ggtcaccatc 60

tcttgttctg gaagcagctc caacatcgga agtaattccg ttagctggta ccagcagctc 120

ccaggaacgg cccccaaact cctcatgtat actaacaatc agcggccctc aggggtccct 180

gaccgattct ctggctccaa gtctggcacc tcagcctccc tggccatcag tgggctccag 240

tctgaggatg aggctgatta ttactgtgcg acatgggatg ccagcctgaa tacttgggtg 300

ttcggcggag ggaccaaggt caccgtccta 330

<210> SEQ ID NO 154
<211> LENGTH: 348
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 154

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 60

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 120

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 180

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 240

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagaggcggg 300

agtgggagtg actactgggg ccaggggaca atggtcaccg tctcgagt 348

<210> SEQ ID NO 155
<211> LENGTH: 330

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 155

aattttatgc tgactcagcc ccactctgtg tcggggtctc cggggaagac ggtaaccatc 60

tcctgcaccc gcagcagtgg ctacattgac agcaagtatg tgcagtggta ccagcagcgc 120

ccgggcagtg cccccaccac tgtgatctat gaggataacc gaagaccctc tggggtccct 180

gatcggttct ctggctccat cgacagctcc tccaactctg cctccctcac catctctgga 240

ctggagactg aggacgaggc tgactattac tgtcagtctt atgatgacac caatgtggtg 300

ttcggcggag ggaccaaggt caccgtccta 330

<210> SEQ ID NO 156
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 156

gaggtccagc tggtgcagtc tggagctgag gtgaaggagc ctggggcctc agtgaaggtc 60

tcctgcaagg cctctggtta cgacttttcc aactatggtt tcagctgggt gcgccaggcc 120

cctggacaag gtcttgagtg gatgggatgg atcagctctt ataatggtta cacaaactat 180

gcacagagac tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 240

atggagctga ggagcctgag atctgacgac acagctgtct attactgtgc gagagatcga 300

ggacttggaa actggtactt cgatctctgg ggccaaggca ccctggtcac cgtctcgagt 360

<210> SEQ ID NO 157
<211> LENGTH: 330
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 157

cagtctgtgc tgactcagcc tgcctccgtg tctgggtctc ctggacagtc gatcaccatc 60

tcctgcactg gaaccagcag tgacgttggt ggttataact atgtctcctg gtaccaacaa 120

cacccaggca aagcccccaa actcatgatt tatgagggca gtaagcggcc ctcaggggtt 180

tctaatcgct tctctggctc caagtctggc aacacggcct ccctgacaat ctctgggctc 240

caggctgagg acgaggctga ttattactgc agctcatata caaccaggag cactcgagtt 300

ttcggcggag ggaccaagct gaccgtccta 330

<210> SEQ ID NO 158
<211> LENGTH: 1518
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 158

atggattttc aagtgcagat tttcagcttc ctgctaatca gtgcttcagt cataatgtcc 60

agaggagata ttcagatgac ccagagcccg agcagcctga gcgcgagcgt gggcgatcgc 120

gtgaccatta cctgccgcgc gagccaggat gtgaacaccg cggtggcgtg gtatcagcag 180

aaaccgggca aagcgccgaa actgctgatt tatagcgcga gctttctgta tagcggcgtg 240

ccgagccgct ttagcggcag ccgcagcggc accgatttta ccctgaccat tagcagcctg 300

cagccggaag attttgcgac ctattattgc cagcagcatt ataccacccc gccgaccttt 360

ggccagggca ccaaagtgga aattaaacgc accgggggtg gaggctctgg tggcggtggc 420

tctggcggag gtggatccgg tggcggcgga tctgaagtgc agctggtgga aagcggcggc 480

ggcctggtgc agccgggcgg cagcctgcgc ctgagctgcg cggcgagcgg ctttaacatt 540

aaagatacct atattcattg ggtgcgccag gcgccgggca aaggcctgga atgggtggcg 600

cgcatttatc cgaccaacgg ctatacccgc tatgcggata gcgtgaaagg ccgctttacc 660

attagcgcgg ataccagcaa aaacaccgcg tatctgcaga tgaacagcct gcgcgcggaa 720

gataccgcgg tgtattattg cagccgctgg ggcggcgatg gcttttatgc gatggattat 780

tggggccagg gcaccctggt gaccgtgagc agtgatcagg agcccaaatc ttgtgacaaa 840

actcacacat ctccaccgtg ctcagcacct gaactcctgg gtggaccgtc agtcttcctc 900

ttcccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg 960

gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt ggacggcgtg 1020

gaggtgcata atgccaagac aaagccgcgg gaggagcagt acaacagcac gtaccgtgtg 1080

gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag 1140

gtctccaaca aagccctccc agccccatc gagaaaacca tctccaaagc caaagggcag 1200

ccccgagaac cacaggtgta caccctgccc ccatcccggg atgagctgac caagaaccag 1260

gtcagcctga cctgcctggt caaaggcttc tatccaagcg acatcgccgt ggagtgggag 1320

agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga ctccgacggc 1380

tccttcttcc tctacagcaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc 1440

ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc 1500

ctgtctccgg gtaaatga 1518

<210> SEQ ID NO 159
<211> LENGTH: 505
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 159

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Met Ser Arg Gly Asp Ile Gln Met Thr Gln Ser Pro Ser Ser
20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser

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35                  40                  45

Gln Asp Val Asn Thr Ala Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys
50                  55                  60

Ala Pro Lys Leu Leu Ile Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val
65                  70                  75                  80

Pro Ser Arg Phe Ser Gly Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr
85                  90                  95

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
100                 105                 110

His Tyr Thr Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile
115                 120                 125

Lys Arg Thr Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly
130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Glu Val Gln Leu Val Glu Ser Gly Gly
145                 150                 155                 160

Gly Leu Val Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser
165                 170                 175

Gly Phe Asn Ile Lys Asp Thr Tyr Ile His Trp Val Arg Gln Ala Pro
180                 185                 190

Gly Lys Gly Leu Glu Trp Val Ala Arg Ile Tyr Pro Thr Asn Gly Tyr
195                 200                 205

Thr Arg Tyr Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Ala Asp
210                 215                 220

Thr Ser Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu
225                 230                 235                 240

Asp Thr Ala Val Tyr Tyr Cys Ser Arg Trp Gly Gly Asp Gly Phe Tyr
245                 250                 255

Ala Met Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Asp
260                 265                 270

Gln Glu Pro Lys Ser Cys Asp Lys Thr His Thr Ser Pro Pro Cys Ser
275                 280                 285

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
290                 295                 300

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
305                 310                 315                 320

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
325                 330                 335

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
340                 345                 350

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
355                 360                 365

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
370                 375                 380

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
385                 390                 395                 400

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
405                 410                 415

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
420                 425                 430

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
435                 440                 445
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Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
450 455 460

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
465 470 475 480

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
485 490 495

Lys Ser Leu Ser Leu Ser Pro Gly Lys
500 505

<210> SEQ ID NO 160
<211> LENGTH: 66
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticoligonucleotide"

<400> SEQUENCE: 160

atggattttc aagtgcagat tttcagcttc ctgctaatca gtgcttcagt cataatgtcc 60

agagga 66

<210> SEQ ID NO 161
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpeptide"

<400> SEQUENCE: 161

Met Asp Phe Gln Val Gln Ile Phe Ser Phe Leu Leu Ile Ser Ala Ser
1 5 10 15

Val Ile Met Ser Arg Gly
20

<210> SEQ ID NO 162
<211> LENGTH: 327
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

<400> SEQUENCE: 162

gatattcaga tgacccagag cccgagcagc ctgagcgcga gcgtgggcga tcgcgtgacc 60

attacctgcc gcgcgagcca ggatgtgaac accgcggtgg cgtggtatca gcagaaaccg 120

ggcaaagcgc cgaaactgct gatttatagc gcgagctttc tgtatagcgg cgtgccgagc 180

cgctttagcg gcagccgcag cggcaccgat ttttaccctga ccattagcag cctgcagccg 240

gaagattttg cgacctatta ttgccagcag cattatacca ccccgccgac ctttggccag 300

ggcaccaaag tggaaattaa acgcacc 327

<210> SEQ ID NO 163
<211> LENGTH: 109
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 163

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asp Val Asn Thr Ala
20 25 30

Val Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Ser Ala Ser Phe Leu Tyr Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Arg Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln His Tyr Thr Thr Pro Pro
85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr
100 105

<210> SEQ ID NO 164
<211> LENGTH: 60
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticoligonucleotide"

<400> SEQUENCE: 164

ggggggtggag gctctggtgg cggtggctct ggcggaggtg gatccggtgg cggcggatct 60

<210> SEQ ID NO 165
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpeptide"

<400> SEQUENCE: 165

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
1 5 10 15

Gly Gly Gly Ser
20

<210> SEQ ID NO 166
<211> LENGTH: 360
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 166

gaagtgcagc tggtggaaag cggcggcggc ctggtgcagc cgggcggcag cctgcgcctg 60

agctgcgcgg cgagcggctt taacattaaa gatacctata ttcattgggt gcgccaggcg 120

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ccgggcaaag gcctggaatg ggtggcgcgc atttatccga ccaacggcta tacccgctat 180

gcggatagcg tgaaaggccg ctttaccatt agcgcggata ccagcaaaaa caccgcgtat 240

ctgcagatga acagcctgcg cgcggaagat accgcggtgt attattgcag ccgctggggc 300

ggcgatggct tttatgcgat ggattattgg ggccagggca ccctggtgac cgtgagcagt 360

<210> SEQ ID NO 167
<211> LENGTH: 120
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 167

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Asn Ile Lys Asp Thr
20 25 30

Tyr Ile His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Arg Ile Tyr Pro Thr Asn Gly Tyr Thr Arg Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Ala Asp Thr Ser Lys Asn Thr Ala Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ser Arg Trp Gly Gly Asp Gly Phe Tyr Ala Met Asp Tyr Trp Gly Gln
100 105 110

Gly Thr Leu Val Thr Val Ser Ser
115 120

<210> SEQ ID NO 168
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticoligonucleotide"

<400> SEQUENCE: 168

gagcccaaat cttgtgacaa aactcacaca tctccaccgt gctca 45

<210> SEQ ID NO 169
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpeptide"

<400> SEQUENCE: 169

Glu Pro Lys Ser Cys Asp Lys Thr His Thr Ser Pro Pro Cys Ser
1 5 10 15

<210> SEQ ID NO 170
<211> LENGTH: 654

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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 170

gcacctgaac tcctgggtgg accgtcagtc ttcctcttcc ccccaaaacc caaggacacc 60

ctcatgatct cccggacccc tgaggtcaca tgcgtggtgg tggacgtgag ccacgaagac 120

cctgaggtca agttcaactg gtacgtggac ggcgtggagg tgcataatgc caagacaaag 180

ccgcgggagg agcagtacaa cagcacgtac cgtgtggtca gcgtcctcac cgtcctgcac 240

caggactggc tgaatggcaa ggagtacaag tgcaaggtct ccaacaaagc cctcccagcc 300

cccatcgaga aaaccatctc caaagccaaa gggcagcccc gagaaccaca ggtgtacacc 360

ctgccccccat cccgggatga gctgaccaag aaccaggtca gcctgacctg cctggtcaaa 420

ggcttctatc caagcgacat cgccgtggag tgggagagca atgggcagcc ggagaacaac 480

tacaagacca cgcctcccgt gctggactcc gacggctcct tcttcctcta cagcaagctc 540

accgtggaca agagcaggtg gcagcagggg aacgtcttct catgctccgt gatgcatgag 600

gctctgcaca accactacac gcagaagagc ctctccctgt ctccgggtaa atga 654

<210> SEQ ID NO 171
<211> LENGTH: 217
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 171

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
1 5 10 15

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
20 25 30

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
35 40 45

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
50 55 60

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
65 70 75 80

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
85 90 95

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
100 105 110

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
115 120 125

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
130 135 140

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
145 150 155 160

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
165 170 175

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Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
180 185 190

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
195 200 205

Lys Ser Leu Ser Leu Ser Pro Gly Lys
210 215

<210> SEQ ID NO 172
<211> LENGTH: 1503
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 172

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtgcagc tggtgcagtc tgggtctgag gtgaggaggc ctgggtcctc ggtgagggtc 120

tcctgcacgg cttctggaga cacctccagc agctttaccg tcaactggct gcgacaggcc 180

cctggacaag gtcttgagtg gatgggaggg atcaccccta tgtttggcac tgcaaactac 240

gcacagatgt tcgaggacag agtcacgata accgcggacg aaatggaact gagtggcctg 300

acatctgagg acacggccgt gtatttttgt gcgacaggcc cctccgatta cgtttggggg 360

agttatcgtt tccttgacac ctgggggcgg gggaccacgg tcaccgtctc gagtggaggc 420

ggcggttcag gcggaggtgg ctctggcggt ggcggaagtg cacaggctgt gctgactcag 480

ccgtcctcag tgtctgcggc cccaggacag gaggtctcca tctcctgctc tggagccaga 540

tccaacgttg ggggtaatta tgtttcctgg taccaacacc tcccaggaac agcccccaaa 600

ctcctcattt atgacaataa taagcgaccc tcagggatgc ctgaccgatt ctctggctcc 660

aagtctggca cgtcagccac cctgggcatc accggagtcc agactgagga cgaggccgat 720

tattactgcg caacatggga tagcagcctg agcgctgtgg tcttcggcgg agggaccaag 780

ctgaccgtcc taggtgacgt acgcgagccc aaatcttctg acaaaactca cacatgccca 840

ccgtgcccag cacctgaact cctgggtgga ccgtcagtct tcctcttccc cccaaaaccc 900

aaggacaccc tcatgatctc ccggaccccct gaggtcacat gcgtggtggt ggacgtgagc 960

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 1020

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 1080

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 1140

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 1200

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc 1260

ctggtcaaag gcttctatcc aagcgacatc gccgtggagt gggagagcaa tgggcagccg 1320

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 1380

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 1440

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 1500

tga 1503

<210> SEQ ID NO 173
<211> LENGTH: 500

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<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 173

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Ser Glu Val Arg
20 25 30

Arg Pro Gly Ser Ser Val Arg Val Ser Cys Thr Ala Ser Gly Asp Thr
35 40 45

Ser Ser Ser Phe Thr Val Asn Trp Leu Arg Gln Ala Pro Gly Gln Gly
50 55 60

Leu Glu Trp Met Gly Gly Ile Thr Pro Met Phe Gly Thr Ala Asn Tyr
65 70 75 80

Ala Gln Met Phe Glu Asp Arg Val Thr Ile Thr Ala Asp Glu Met Glu
85 90 95

Leu Ser Gly Leu Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Thr
100 105 110

Gly Pro Ser Asp Tyr Val Trp Gly Ser Tyr Arg Phe Leu Asp Thr Trp
115 120 125

Gly Arg Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ala Val Leu Thr Gln
145 150 155 160

Pro Ser Ser Val Ser Ala Ala Pro Gly Gln Glu Val Ser Ile Ser Cys
165 170 175

Ser Gly Ala Arg Ser Asn Val Gly Gly Asn Tyr Val Ser Trp Tyr Gln
180 185 190

His Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Asp Asn Asn Lys
195 200 205

Arg Pro Ser Gly Met Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr
210 215 220

Ser Ala Thr Leu Gly Ile Thr Gly Val Gln Thr Glu Asp Glu Ala Asp
225 230 235 240

Tyr Tyr Cys Ala Thr Trp Asp Ser Ser Leu Ser Ala Val Val Phe Gly
245 250 255

Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser
260 265 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
275 280 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
290 295 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305 310 315 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
325 330 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
340 345 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn

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355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385                 390                 395                 400

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
405                 410                 415

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
485                 490                 495

Ser Pro Gly Lys
500


<210> SEQ ID NO 174
<211> LENGTH: 1503
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolynucleotide"

<400> SEQUENCE: 174

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

caggtgcagc tggtgcagtc tgggtctgag gtgaggaggc ctgggtcctc ggtgaggatc    120

tcctgcacgg cttctggaga cacctccagc agctttaccg tcaactgggt gcgacaggcc    180

cctggacaag gtcttgagtg gatgggaggg atcaccccta tgtttggcac tgcaaactac    240

gcacaggtgt tcgaggacag agtcacaata atcgcggacg agatggaact gagtggcctg    300

acatctgagg acacggccgt gtatttctgt gcgacaggcc cctccgatta cgtttggggg    360

agttatcgtt tccttgacaa ctggggcagg ggcaccctgg tcaccgtctc gagtggaggc    420

ggcggttcag gcggaggtgg ctctggcggt ggcggaagtg cacagtctgt gctgactcag    480

ccaccctcag tgtctgcggc cccagggcag aaggtcacca tctcctgctc tggaggcagg    540

tccagcattg ggaataatta tgtgtcctgg tatcaacacc tcccaggaac agcccccaaa    600

ctcctcatct atgacaataa tcagcgaccc tcagggattc ctgaccgatt ctctggctcc    660

aagtctggca cgtcagccac cctgggcatc accggactcc agactgggga cgaggccgat    720

tattactgcg gaacatggga tagcagcctg agtgctgtgg tgtttggcgg agggaccaag    780

gtcaccgtcc taggtgacgt acgcgagccc aaatcttctg acaaaactca cacatgccca    840

ccgtgcccag cacctgaact cctgggtgga ccgtcagtct tcctcttccc cccaaaaccc    900

aaggacaccc tcatgatctc ccggaccccc gaggtcacat gcgtggtggt ggacgtgagc    960

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc   1020

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc   1080
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gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 1140

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 1200

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc 1260

ctggtcaaag gcttctatcc aagcgacatc gccgtggagt gggagagcaa tgggcagccg 1320

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 1380

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 1440

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 1500

tga 1503

<210> SEQ ID NO 175
<211> LENGTH: 500
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 175

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Gln Val Gln Leu Val Gln Ser Gly Ser Glu Val Arg
20 25 30

Arg Pro Gly Ser Ser Val Arg Ile Ser Cys Thr Ala Ser Gly Asp Thr
35 40 45

Ser Ser Ser Phe Thr Val Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
50 55 60

Leu Glu Trp Met Gly Gly Ile Thr Pro Met Phe Gly Thr Ala Asn Tyr
65 70 75 80

Ala Gln Val Phe Glu Asp Arg Val Thr Ile Ile Ala Asp Glu Met Glu
85 90 95

Leu Ser Gly Leu Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Thr
100 105 110

Gly Pro Ser Asp Tyr Val Trp Gly Ser Tyr Arg Phe Leu Asp Asn Trp
115 120 125

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser Val Leu Thr Gln
145 150 155 160

Pro Pro Ser Val Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys
165 170 175

Ser Gly Gly Arg Ser Ser Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln
180 185 190

His Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Asp Asn Asn Gln
195 200 205

Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr
210 215 220

Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln Thr Gly Asp Glu Ala Asp
225 230 235 240

Tyr Tyr Cys Gly Thr Trp Asp Ser Ser Leu Ser Ala Val Val Phe Gly
245 250 255

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Gly Gly Thr Lys Val Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser
260 265 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
275 280 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
290 295 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305 310 315 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
325 330 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
340 345 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
355 360 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
370 375 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385 390 395 400

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
405 410 415

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
420 425 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
435 440 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
450 455 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465 470 475 480

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
485 490 495

Ser Pro Gly Lys
500

<210> SEQ ID NO 176
<211> LENGTH: 1515
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 176

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaagtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 120

tcctgcaagg cttctgggta cagcttcacc gccttctata ttcactgggt gcgacaggcc 180

cctggacaag gccttgagta tttgggatgg atcgacccta atactggtgc cacaaaatat 240

gcacagcgct ttcagggcag ggtcatcatg acctgggaca cgtccatcac cacagccacc 300

atggaactga gcaggctgac gtctgacgac tcggccgtct actactgtgt gagagatttg 360

cgggagtggg gctacgaatt gtccgttgag tattggggca gaggaaccct ggtcaccgtc 420

tcgagtggag gcggcggttc aggcggaggt ggctctggcg gtggcggaag tgcacagtct 480

-continued

gtgctgactc agccaccctc agcgtctggg acccccgggc agagggtcac catctcttgt 540

tctggaagca gctccaacat cggaagtaat tatgtatact ggtaccagca gctcccagga 600

acggccccca aactcctcat ctataggaat aatcagcggc cctcaggggt ccctgaccga 660

ttctctggct ccaagtctgg cacctcagcc tccctggcca tcagtgggct ccggtccgag 720

gatgaggctg attattactg tgcagcatgg gatgacagcc tgagtggttg ggtgttcggc 780

ggagggacca agctgaccgt cctaggtgac gtacgcgagc ccaaatcttc tgacaaaact 840

cacacatgcc caccgtgccc agcacctgaa ctcctgggtg gaccgtcagt cttcctcttc 900

cccccaaaac ccaaggacac cctcatgatc tcccggaccc ctgaggtcac atgcgtggtg 960

gtggacgtga gccacgaaga ccctgaggtc aagttcaact ggtacgtgga cggcgtggag 1020

gtgcataatg ccaagacaaa gccgcgggag gagcagtaca acagcacgta ccgtgtggtc 1080

agcgtcctca ccgtcctgca ccaggactgg ctgaatggca aggagtacaa gtgcaaggtc 1140

tccaacaaag ccctcccagc ccccatcgag aaaaccatct ccaaagccaa agggcagccc 1200

cgagaaccac aggtgtacac cctgccccca tcccgggatg agctgaccaa gaaccaggtc 1260

agcctgacct gcctggtcaa aggcttctat ccaagcgaca tcgccgtgga gtgggagagc 1320

aatgggcagc cggagaacaa ctacaagacc acgcctcccg tgctggactc cgacggctcc 1380

ttcttcctct acagcaagct caccgtggac aagagcaggt ggcagcaggg gaacgtcttc 1440

tcatgctccg tgatgcatga ggctctgcac aaccactaca cgcagaagag cctctccctg 1500

tctccgggta aatga 1515

<210> SEQ ID NO 177
<211> LENGTH: 504
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 177

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
20 25 30

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ser
35 40 45

Phe Thr Ala Phe Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly
50 55 60

Leu Glu Tyr Leu Gly Trp Ile Asp Pro Asn Thr Gly Ala Thr Lys Tyr
65 70 75 80

Ala Gln Arg Phe Gln Gly Arg Val Ile Met Thr Trp Asp Thr Ser Ile
85 90 95

Thr Thr Ala Thr Met Glu Leu Ser Arg Leu Thr Ser Asp Asp Ser Ala
100 105 110

Val Tyr Tyr Cys Val Arg Asp Leu Arg Glu Trp Gly Tyr Glu Leu Ser
115 120 125

Val Glu Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly
130 135 140

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Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser
145                 150                 155                 160

Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln Arg Val
165                 170                 175

Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Tyr Val
180                 185                 190

Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr
195                 200                 205

Arg Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser
210                 215                 220

Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg Ser Glu
225                 230                 235                 240

Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu Ser Gly
245                 250                 255

Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg
260                 265                 270

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
275                 280                 285

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
290                 295                 300

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
305                 310                 315                 320

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
325                 330                 335

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
340                 345                 350

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
355                 360                 365

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
370                 375                 380

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
385                 390                 395                 400

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
405                 410                 415

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
420                 425                 430

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
435                 440                 445

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
450                 455                 460

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
465                 470                 475                 480

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
485                 490                 495

Ser Leu Ser Leu Ser Pro Gly Lys
500
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<210> SEQ ID NO 178
<211> LENGTH: 1503
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source

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<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 178

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 120

tcctgcaagg cttctggata caccttcacc ggctactata tgcactgggt gcgacaggcc 180

cctggacaag ggcttgagtg gatgggatgg atcaacccta acagtggtgg cacaaactat 240

gcacagaagt ttcagggctg ggtcaccatg accagggaca cgtccatcag cacagcctac 300

atggagctga gcaggctgag atctgacgac acggccgtgt attactgtgc gagagattct 360

actatggccc caggtgcttt tgatatctgg ggccgaggca ccctggtcac cgtctcgagt 420

ggaggcggcg gttcaggcgg aggtggctct ggcggtggcg gaagtgcaca gtctgtgctg 480

actcagccac cctcggtgtc agtggcccca ggacagacgg ccaggatgac ctgtggggga 540

aacaacattg aaagtaaaac tgtgcattgg taccagcaga agccgggcca ggcccctgtg 600

ctggtcgtct acaatgataa cgtccggccc tcagggatcc ctgcgcgatt ctctggctcc 660

aactccggca acacggccac cctgaccatc aacagggtcg aagccgggga tgaggccgac 720

tattattgtc aggtgtggga ctccagtaga gatcaagggg tattcggcgg agggaccaag 780

ctgaccgtcc taggtgacgt acgcgagccc aaatcttctg acaaaactca cacatgccca 840

ccgtgcccag cacctgaact cctgggtgga ccgtcagtct tcctcttccc cccaaaaccc 900

aaggacaccc tcatgatctc ccggaccct gaggtcacat gcgtggtggt ggacgtgagc 960

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 1020

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 1080

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 1140

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 1200

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc 1260

ctggtcaaag gcttctatcc aagcgacatc gccgtggagt gggagagcaa tgggcagccg 1320

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 1380

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 1440

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 1500

tga 1503

<210> SEQ ID NO 179
<211> LENGTH: 500
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 179

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
20 25 30

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr

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35                  40                  45

Phe Thr Gly Tyr Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly
50                  55                  60

Leu Glu Trp Met Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr
65                  70                  75                  80

Ala Gln Lys Phe Gln Gly Trp Val Thr Met Thr Arg Asp Thr Ser Ile
85                  90                  95

Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala
100                 105                 110

Val Tyr Tyr Cys Ala Arg Asp Ser Thr Met Ala Pro Gly Ala Phe Asp
115                 120                 125

Ile Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser Val Leu
145                 150                 155                 160

Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Met
165                 170                 175

Thr Cys Gly Gly Asn Asn Ile Glu Ser Lys Thr Val His Trp Tyr Gln
180                 185                 190

Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr Asn Asp Asn Val
195                 200                 205

Arg Pro Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser Asn Ser Gly Asn
210                 215                 220

Thr Ala Thr Leu Thr Ile Asn Arg Val Glu Ala Gly Asp Glu Ala Asp
225                 230                 235                 240

Tyr Tyr Cys Gln Val Trp Asp Ser Ser Arg Asp Gln Gly Val Phe Gly
245                 250                 255

Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser
260                 265                 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
275                 280                 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385                 390                 395                 400

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
405                 410                 415

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
435                 440                 445
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Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
485                 490                 495

Ser Pro Gly Lys
500


<210> SEQ ID NO 180
<211> LENGTH: 1503
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolynucleotide"

<400> SEQUENCE: 180

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

gaggtgcagc tggtgcagtc tgggggaggc ttggtcaggc ctggagggtc cctgagactc    120

tcctgtgcag cctcgggatt ctccttcagt gactactaca tgacctggat ccgccagatt    180

ccagggaagg ggctggagtg ggtggcagtt atatggaatg atggaagtga tagatactat    240

gcagactccg tgaagggccg attcaccatt tccagagaca attccaagaa cacgctgttt    300

ctgcaaatga gcagcctgag agacgaggac acggctctat attactgtgt gagaggggga    360

ccaacagctt caagcggatt tgactactgg ggccgaggca ccctggtcac cgtctcgagt    420

ggtggaggcg gttcaggcgg aggtggcagc ggcggtggcg gatcgtctga gctgactcag    480

cctgcctccg tgtctgggtc tcctggacag tcgatcacca tctcctgcac tggaaccagc    540

agtgacgttg gtggttataa ctatgtctcc tggtacctac aacacccagg caaagccccc    600

aaactcatga tttatgaggg cagtaagcgg ccctcagggg tttctaatcg cttctctggc    660

tccaagtctg gcaacacggc ctccctgaca atctctgggc tccaggctga ggacgaggct    720

gattattact gcagctcata tacaaccagg agcactcgag ttttcggcgg agggaccaag    780

ctgaccgtcc taggtgacgt acgcgagccc aaatcttctg acaaaactca cacatgccca    840

ccgtgcccag cacctgaact cctgggtgga ccgtcagtct tcctcttccc cccaaaaccc    900

aaggacaccc tcatgatctc ccggaccccc gaggtcacat gcgtggtggt ggacgtgagc    960

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc   1020

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc   1080

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc   1140

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag   1200

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc   1260

ctggtcaaag gcttctatcc aagcgacatc gccgtggagt gggagagcaa tgggcagccg   1320

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac   1380

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg   1440

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa   1500

tga                                                                 1503
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<210> SEQ ID NO 181
<211> LENGTH: 500
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 181

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val
20 25 30

Arg Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser
35 40 45

Phe Ser Asp Tyr Tyr Met Thr Trp Ile Arg Gln Ile Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ala Val Ile Trp Asn Asp Gly Ser Asp Arg Tyr Tyr
65 70 75 80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85 90 95

Asn Thr Leu Phe Leu Gln Met Ser Ser Leu Arg Asp Glu Asp Thr Ala
100 105 110

Leu Tyr Tyr Cys Val Arg Gly Gly Pro Thr Ala Ser Ser Gly Phe Asp
115 120 125

Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Glu Leu Thr Gln
145 150 155 160

Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys
165 170 175

Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr
180 185 190

Leu Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu Gly Ser
195 200 205

Lys Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly
210 215 220

Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala
225 230 235 240

Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg Ser Thr Arg Val Phe Gly
245 250 255

Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser
260 265 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
275 280 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
290 295 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305 310 315 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
325 330 335

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Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385                 390                 395                 400

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
405                 410                 415

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
485                 490                 495

Ser Pro Gly Lys
500


<210> SEQ ID NO 182
<211> LENGTH: 1503
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolynucleotide"

<400> SEQUENCE: 182

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

caggtgcagc tgcaggagtc gggtccagga ctggtgaagc cctcgcagac cttgtcactc    120

acctgtggca tctccgggga cagtgtctct agcaacagtg ctgcttggaa ctggatcagg    180

cagtccccaa cgagaggcct tgagtggctg ggaaggacat attacaggtc cagttggtat    240

cataactatg caccttctat gaacagtcga ttaaccatca tcgcagacac atccaaaaac    300

cagttctctt tgcaactgaa ctctgtgact cccgaggaca cggctgtata ttactgtgca    360

agcgggtggg cctttgatgt ctggggcagg ggaaccctgg tcaccgtctc gagtggaggc    420

ggcggttcag gcggaggtgg ctctggcggt ggcggaagtg cacagtctgt gctgactcag    480

ccaccctccg cgtccgggtc tcctggacag tcagtcacca tctcctgcac tggaaccagc    540

agtgacgttg gtgcttatga ctttgtctcc tggtaccaac agcaccctgg caaagccccc    600

aaactcatga tttatgaggt caataagcgg ccctcagggg tccctgatcg cttctctggc    660

tccaagtctg gcaacacggc ctccctgacc gtctctgggc tccaggctga ggatgaggct    720

gattattact gcagctcata tgcaggcagc aagaatttgc ttttcggcgg agggaccaag    780

ctgaccgtcc taggtgacgt acgcgagccc aaatcttctg acaaaactca cacatgccca    840

ccgtgcccag cacctgaact cctgggtgga ccgtcagtct tcctcttccc cccaaaaccc    900

aaggacaccc tcatgatctc ccggacccct gaggtcacat gcgtggtggt ggacgtgagc    960
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cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 1020

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 1080

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 1140

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 1200

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc 1260

ctggtcaaag gcttctatcc aagcgacatc gccgtggagt gggagagcaa tgggcagccg 1320

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 1380

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 1440

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 1500

tga 1503

<210> SEQ ID NO 183
<211> LENGTH: 500
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 183

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val
20 25 30

Lys Pro Ser Gln Thr Leu Ser Leu Thr Cys Gly Ile Ser Gly Asp Ser
35 40 45

Val Ser Ser Asn Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Thr
50 55 60

Arg Gly Leu Glu Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Ser Trp Tyr
65 70 75 80

His Asn Tyr Ala Pro Ser Met Asn Ser Arg Leu Thr Ile Ile Ala Asp
85 90 95

Thr Ser Lys Asn Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu
100 105 110

Asp Thr Ala Val Tyr Tyr Cys Ala Ser Gly Trp Ala Phe Asp Val Trp
115 120 125

Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser Val Leu Thr Gln
145 150 155 160

Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln Ser Val Thr Ile Ser Cys
165 170 175

Thr Gly Thr Ser Ser Asp Val Gly Ala Tyr Asp Phe Val Ser Trp Tyr
180 185 190

Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu Val Asn
195 200 205

Lys Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly
210 215 220

Asn Thr Ala Ser Leu Thr Val Ser Gly Leu Gln Ala Glu Asp Glu Ala

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225 230 235 240

Asp Tyr Tyr Cys Ser Ser Tyr Ala Gly Ser Lys Asn Leu Leu Phe Gly
245 250 255

Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser
260 265 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
275 280 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
290 295 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305 310 315 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
325 330 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
340 345 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
355 360 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
370 375 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385 390 395 400

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
405 410 415

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
420 425 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
435 440 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
450 455 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465 470 475 480

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
485 490 495

Ser Pro Gly Lys
500

<210> SEQ ID NO 184
<211> LENGTH: 1506
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 184

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggtc cctgagactc 120

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 180

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 240

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 300

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagaggatac 360

-continued

agtggctacg atgaccctga ctcctggggg agagggacca cggtcaccgt ctcgagtgga 420

ggcggcggtt caggcggagg tggctctggc ggtggcggaa gtgcacacgt tatactgact 480

caaccgccct caacgtctgg gacccccggg cagacggtca ccatctcttg ttctgggagc 540

agctccaaca tcggaagtca ttatgtatac tggtaccagc agctcccagg aacggccccc 600

aaactcctca tctataggaa taatcagcgg ccctcagggg tccctgaccg attctctggc 660

tccaagtctg gcacctcagc ctccctggcc atcagtgggc tccggtccga ggatgagact 720

gattattact gtgcagcatg ggatgacagc ctgagtggtc gagtcttcgg aactgggacc 780

aagctgaccg tcctaggtga cgtacgcgag cccaaatctt ctgacaaaac tcacacatgc 840

ccaccgtgcc cagcacctga actcctgggt ggaccgtcag tcttcctctt cccccaaaa 900

cccaaggaca ccctcatgat ctcccggacc cctgaggtca catgcgtggt ggtggacgtg 960

agccacgaag accctgaggt caagttcaac tggtacgtgg acggcgtgga ggtgcataat 1020

gccaagacaa agccgcggga ggagcagtac aacagcacgt accgtgtggt cagcgtcctc 1080

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa 1140

gccctcccag cccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca 1200

caggtgtaca ccctgccccc atcccgggat gagctgacca agaaccaggt cagcctgacc 1260

tgcctggtca aaggcttcta tccaagcgac atcgccgtgg agtgggagag caatgggcag 1320

ccggagaaca actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc 1380

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc 1440

gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctccgggt 1500

aaatga 1506

<210> SEQ ID NO 185
<211> LENGTH: 501
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 185

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val
20 25 30

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Arg Gly Tyr Ser Gly Tyr Asp Asp Pro Asp Ser
115 120 125

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Trp Gly Arg Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala His Val Ile Leu Thr
145                 150                 155                 160

Gln Pro Pro Ser Thr Ser Gly Thr Pro Gly Gln Thr Val Thr Ile Ser
165                 170                 175

Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser His Tyr Val Tyr Trp Tyr
180                 185                 190

Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Arg Asn Asn
195                 200                 205

Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly
210                 215                 220

Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg Ser Glu Asp Glu Thr
225                 230                 235                 240

Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu Ser Gly Arg Val Phe
245                 250                 255

Gly Thr Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys
260                 265                 270

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
275                 280                 285

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
290                 295                 300

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
305                 310                 315                 320

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
325                 330                 335

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
340                 345                 350

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
355                 360                 365

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
370                 375                 380

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
385                 390                 395                 400

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
405                 410                 415

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
420                 425                 430

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
435                 440                 445

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
450                 455                 460

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
465                 470                 475                 480

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
485                 490                 495

Leu Ser Pro Gly Lys
500


<210> SEQ ID NO 186
<211> LENGTH: 1497
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<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 186

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

caggtacagc tgcagcagtc aggggctgag gtgaagaagc ctgggtcctc ggtgaaggtc 120

tcctgcaagg cttctggagg caccatcagc aactatgcta tcagttgggt gcggctggcc 180

cctggacaag gtcttgagtg gatgggaagt atcgtccctc ttcatgggac aacaaacttc 240

gcacagaaat tccagggcag agtcacgatc accgcggacg agtccacgag cacatcctac 300

atggaggtga acgtcctgac atatgaagac acggcgatgt attattgtgc gtctctcaat 360

tggggctact ggggccgggg caccctggtc accgtctcga gtggaggcgg cggttcaggc 420

ggaggtggct ctggcggtgg cggaagtgca cttaatttta tgctgactca gccccactct 480

gtgtcggagt ctccggggaa gacggtaacc atctcctgca ccggcagtag tggcagcatt 540

gccagcaact atgtgcagtg gtaccagcag cgcccggaca gtgcccccac cactgtgatc 600

tatgaggata atcgaagatc ctctggagtc cctgatcggt tctctggctc catcgacagc 660

tcctccaact ctgcctccct cagcatctct ggactgaaga ctgaggacga ggctgactac 720

tactgtcagt cctatgatag tagcggtcat gtggtcttcg gcggagggac caagctgacc 780

gtcctaggtg acgtacgcga gcccaaatct tctgacaaaa ctcacacatg cccaccgtgc 840

ccagcacctg aactcctggg tggaccgtca gtcttcctct tccccccaaa acccaaggac 900

accctcatga tctcccggac ccctgaggtc acatgcgtgg tggtggacgt gagccacgaa 960

gaccctgagg tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca 1020

aagccgcggg aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg 1080

caccaggact ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctccca 1140

gcccccatcg agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac 1200

accctgcccc catcccggga tgagctgacc aagaaccagg tcagcctgac ctgcctggtc 1260

aaaggcttct atccaagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac 1320

aactacaaga ccacgcctcc cgtgctggac tccgacggct ccttcttcct ctacagcaag 1380

ctcaccgtgg acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat 1440

gaggctctgc acaaccacta cacgcagaag agcctctccc tgtctccggg taaatga 1497

<210> SEQ ID NO 187
<211> LENGTH: 498
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 187

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Val Lys
20 25 30

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Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr
35                  40                  45

Ile Ser Asn Tyr Ala Ile Ser Trp Val Arg Leu Ala Pro Gly Gln Gly
50                  55                  60

Leu Glu Trp Met Gly Ser Ile Val Pro Leu His Gly Thr Thr Asn Phe
65                  70                  75                  80

Ala Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr
85                  90                  95

Ser Thr Ser Tyr Met Glu Val Asn Val Leu Thr Tyr Glu Asp Thr Ala
100                 105                 110

Met Tyr Tyr Cys Ala Ser Leu Asn Trp Gly Tyr Trp Gly Arg Gly Thr
115                 120                 125

Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
130                 135                 140

Gly Gly Gly Gly Ser Ala Leu Asn Phe Met Leu Thr Gln Pro His Ser
145                 150                 155                 160

Val Ser Glu Ser Pro Gly Lys Thr Val Thr Ile Ser Cys Thr Gly Ser
165                 170                 175

Ser Gly Ser Ile Ala Ser Asn Tyr Val Gln Trp Tyr Gln Gln Arg Pro
180                 185                 190

Asp Ser Ala Pro Thr Thr Val Ile Tyr Glu Asp Asn Arg Arg Ser Ser
195                 200                 205

Gly Val Pro Asp Arg Phe Ser Gly Ser Ile Asp Ser Ser Ser Asn Ser
210                 215                 220

Ala Ser Leu Ser Ile Ser Gly Leu Lys Thr Glu Asp Glu Ala Asp Tyr
225                 230                 235                 240

Tyr Cys Gln Ser Tyr Asp Ser Ser Gly His Val Val Phe Gly Gly Gly
245                 250                 255

Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser Ser Asp
260                 265                 270

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
275                 280                 285

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
290                 295                 300

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
305                 310                 315                 320

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
325                 330                 335

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
340                 345                 350

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
355                 360                 365

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
370                 375                 380

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
385                 390                 395                 400

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
405                 410                 415

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
420                 425                 430
```

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```
Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
435                 440                 445

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
450                 455                 460

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
465                 470                 475                 480

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
485                 490                 495

Gly Lys
```

<210> SEQ ID NO 188
<211> LENGTH: 1506
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 188

```
atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

gaggtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggggagtc tctgaagatc    120

tcctgtaagg gttttggata caattttcgc agcgcctgga tcggctgggt gcgccagatg    180

cccggcaaag gcctggagtg gatgggggtc atctatcctg gtgactctga tgtcagatac    240

agtccgtcct tccaaggcca ggtcaccatc tcagccgaca agtccatcag taccgcctac    300

ctgcagtgga gcagcctgaa agcctcggac accgccatgt attattgtac gagacccgta    360

gggcagtggg tggactctga ctattggggc aagggaaccc tggtcaccgt ctcgagtgga    420

ggcggcggtt caggcggagg tggctctggc ggtggcggaa gtgcacagtc tgtgttgacg    480

cagccgccct cagcgtctgg gacccccgga cagagggtca ccatctcttg ttctggaagc    540

agctccaaca tcggaactaa tactgtgaac tggtaccagc agcttccagg aacggccccc    600

aaactcctca tctatactag taatcagcgg ccctcagggg tccctgcccg cttctctgcc    660

tccaactctg gcacctcagc ctccctggcc atcagtgggc tccggtccga ggatgaggct    720

gattattatt gtgcagcgtg ggatgacaag ttgagtggtg cggtgttcgg cggagggacc    780

aagctgaccg tcctaggtga cgtacgcgag cccaaatctt ctgacaaaac tcacacatgc    840

ccaccgtgcc cagcacctga actcctgggt ggaccgtcag tcttcctctt ccccccaaaa    900

cccaaggaca ccctcatgat ctcccggacc cctgaggtca catgcgtggt ggtggacgtg    960

agccacgaag accctgaggt caagttcaac tggtacgtgg acggcgtgga ggtgcataat   1020

gccaagacaa agccgcggga ggagcagtac aacagcacgt accgtgtggt cagcgtcctc   1080

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa   1140

gccctcccag ccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca   1200

caggtgtaca ccctgccccc atcccgggat gagctgacca agaaccaggt cagcctgacc   1260

tgcctggtca aaggcttcta tccaagcgac atcgccgtgg agtgggagag caatgggcag   1320

ccggagaaca actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc   1380

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc   1440

gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctccgggt   1500
```

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aaatga 1506

<210> SEQ ID NO 189
<211> LENGTH: 501
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 189

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
20 25 30

Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Phe Gly Tyr Asn
35 40 45

Phe Arg Ser Ala Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly
50 55 60

Leu Glu Trp Met Gly Val Ile Tyr Pro Gly Asp Ser Asp Val Arg Tyr
65 70 75 80

Ser Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile
85 90 95

Ser Thr Ala Tyr Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala
100 105 110

Met Tyr Tyr Cys Thr Arg Pro Val Gly Gln Trp Val Asp Ser Asp Tyr
115 120 125

Trp Gly Lys Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser Val Leu Thr
145 150 155 160

Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln Arg Val Thr Ile Ser
165 170 175

Cys Ser Gly Ser Ser Ser Asn Ile Gly Thr Asn Thr Val Asn Trp Tyr
180 185 190

Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Thr Ser Asn
195 200 205

Gln Arg Pro Ser Gly Val Pro Ala Arg Phe Ser Ala Ser Asn Ser Gly
210 215 220

Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg Ser Glu Asp Glu Ala
225 230 235 240

Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Lys Leu Ser Gly Ala Val Phe
245 250 255

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys
260 265 270

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
275 280 285

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
290 295 300

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
305 310 315 320

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
325 330 335

-continued

```
Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
340                 345                 350

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
355                 360                 365

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
370                 375                 380

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
385                 390                 395                 400

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
405                 410                 415

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
420                 425                 430

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
435                 440                 445

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
450                 455                 460

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
465                 470                 475                 480

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
485                 490                 495

Leu Ser Pro Gly Lys
500
```

<210> SEQ ID NO 190
<211> LENGTH: 1509
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 190

```
atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc    120

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct    180

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac    240

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat    300

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagacagtcg    360

ggcgcggact ggtacttcga tctctggggc cgaggcaccc tggtcaccgt ctcgagtgga    420

ggcggcggtt caggcggagg tggctctggc ggtggcggaa gtgcacaggc tgtgctgact    480

cagccgtccg cagtttctgg ggccccaggg cagagggtca ccatctcctg cactgggacc    540

agctccaaca tcgggacaaa ctatcttgta cactggtatc agcaacgtcc aggaacagcc    600

ccccaactcc tcgtctctgg taacaacact cgaccctctg gggtcactga ccggttctct    660

gtctccaagt ctgccacttc agcctccctg gccatcactg ggctccaggc tgaggatgag    720

gctgattatt actgccagac ctatgacatc aacttgaggg tttgggtgtt cggcggaggg    780

accaaggtca ccgtcctagg tgacgtacgc gagcccaaat cttctgacaa aactcacaca    840

tgcccaccgt gcccagcacc tgaactcctg ggtggaccgt cagtcttcct cttccccca     900
```

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aaacccaagg acaccctcat gatctcccgg acccctgagg tcacatgcgt ggtggtggac 960

gtgagccacg aagaccctga ggtcaagttc aactggtacg tggacggcgt ggaggtgcat 1020

aatgccaaga caaagccgcg ggaggagcag tacaacagca cgtaccgtgt ggtcagcgtc 1080

ctcaccgtcc tgcaccagga ctggctgaat ggcaaggagt acaagtgcaa ggtctccaac 1140

aaagccctcc cagccccat cgagaaaacc atctccaaag ccaaagggca gccccgagaa 1200

ccacaggtgt acaccctgcc cccatcccgg gatgagctga ccaagaacca ggtcagcctg 1260

acctgcctgg tcaaaggctt ctatccaagc gacatcgccg tggagtggga gagcaatggg 1320

cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctccttcttc 1380

ctctacagca agctcaccgt ggacaagagc aggtggcagc aggggaacgt cttctcatgc 1440

tccgtgatgc atgaggctct gcacaaccac tacacgcaga agagcctctc cctgtctccg 1500

ggtaaatga 1509

<210> SEQ ID NO 191
<211> LENGTH: 502
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 191

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val
20 25 30

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Arg Gln Ser Gly Ala Asp Trp Tyr Phe Asp Leu
115 120 125

Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ala Val Leu Thr
145 150 155 160

Gln Pro Ser Ala Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser
165 170 175

Cys Thr Gly Thr Ser Ser Asn Ile Gly Thr Asn Tyr Leu Val His Trp
180 185 190

Tyr Gln Gln Arg Pro Gly Thr Ala Pro Gln Leu Leu Val Ser Gly Asn
195 200 205

Asn Thr Arg Pro Ser Gly Val Thr Asp Arg Phe Ser Val Ser Lys Ser
210 215 220

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```
Ala Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu
225                 230                 235                 240

Ala Asp Tyr Tyr Cys Gln Thr Tyr Asp Ile Asn Leu Arg Val Trp Val
245                 250                 255

Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Asp Val Arg Glu Pro
260                 265                 270

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
275                 280                 285

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
290                 295                 300

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
305                 310                 315                 320

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
325                 330                 335

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
340                 345                 350

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
355                 360                 365

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
370                 375                 380

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
385                 390                 395                 400

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
405                 410                 415

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
420                 425                 430

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
435                 440                 445

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
450                 455                 460

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
465                 470                 475                 480

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
485                 490                 495

Ser Leu Ser Pro Gly Lys
500
```

<210> SEQ ID NO 192
<211> LENGTH: 1491
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 192

```
atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

gaggtgcagc tggtggagac tggggggaggc gtggtccagc ctgggggggtc cctgagcctc    120

tcctgtgcag cgtctggatt caccttcagt agctatggca tgcagtgggt ccgccaggct    180

ccaggcaagg ggctggagtg ggtggcgttt atacggtacg atggaagtag tgaatactat    240

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat    300
```

-continued

```
ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgg aagaacgctg    360

gagtctagtt tgtggggcaa gggaaccctg gtcaccgtct cgagtggtgg aggcggttca    420

ggcggaggtg gcagcggcgg tggcggatcg cagtctgtgt tgacgcagcc gccctcagtg    480

tctgcggccc caggacagaa ggtcaccatt tcctgctctg gaagcacctc caacattggg    540

aataattatg tctcctggta ccaacagcac ccaggcaaag cccccaaact catgatttat    600

gatgtcagta agcggccctc aggggtccct gaccgattct ctggctccaa gtctggcaac    660

tcagcctccc tggacatcag tgggctccag tctgaggatg aggctgatta ttactgtgca    720

gcatgggatg acagcctgag tgaatttctc ttcggaacta ggaccaagct gaccgtccta    780

ggtgacgtac gcgagcccaa atcttctgac aaaactcaca catgcccacc gtgcccagca    840

cctgaactcc tgggtggacc gtcagtcttc ctcttccccc caaaacccaa ggacaccctc    900

atgatctccc ggacccctga ggtcacatgc gtggtggtgg acgtgagcca cgaagaccct    960

gaggtcaagt tcaactggta cgtggacggc gtggaggtgc ataatgccaa gacaaagccg   1020

cgggaggagc agtacaacag cacgtaccgt gtggtcagcg tcctcaccgt cctgcaccag   1080

gactggctga atggcaagga gtacaagtgc aaggtctcca acaaagccct cccagccccc   1140

atcgagaaaa ccatctccaa agccaaaggg cagccccgag aaccacaggt gtacaccctg   1200

cccccatccc gggatgagct gaccaagaac caggtcagcc tgacctgcct ggtcaaaggc   1260

ttctatccaa gcgacatcgc cgtggagtgg gagagcaatg ggcagccgga gaacaactac   1320

aagaccacgc ctcccgtgct ggactccgac ggctccttct tcctctacag caagctcacc   1380

gtggacaaga gcaggtggca gcaggggaac gtcttctcat gctccgtgat gcatgaggct   1440

ctgcacaacc actacacgca gaagagcctc tccctgtctc cgggtaaatg a            1491
```

<210> SEQ ID NO 193
<211> LENGTH: 496
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 193

```
Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1               5                   10                  15

Asp Thr Thr Gly Glu Val Gln Leu Val Glu Thr Gly Gly Gly Val Val
20                  25                  30

Gln Pro Gly Gly Ser Leu Ser Leu Ser Cys Ala Ala Ser Gly Phe Thr
35                  40                  45

Phe Ser Ser Tyr Gly Met Gln Trp Val Arg Gln Ala Pro Gly Lys Gly
50                  55                  60

Leu Glu Trp Val Ala Phe Ile Arg Tyr Asp Gly Ser Ser Glu Tyr Tyr
65                  70                  75                  80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100                 105                 110

Val Tyr Tyr Cys Gly Arg Thr Leu Glu Ser Ser Leu Trp Gly Lys Gly
115                 120                 125
```

-continued

```
Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
130                 135                 140

Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Pro Ser Val
145                 150                 155                 160

Ser Ala Ala Pro Gly Gln Lys Val Thr Ile Ser Cys Ser Gly Ser Thr
165                 170                 175

Ser Asn Ile Gly Asn Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly
180                 185                 190

Lys Ala Pro Lys Leu Met Ile Tyr Asp Val Ser Lys Arg Pro Ser Gly
195                 200                 205

Val Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Asn Ser Ala Ser Leu
210                 215                 220

Asp Ile Ser Gly Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala
225                 230                 235                 240

Ala Trp Asp Asp Ser Leu Ser Glu Phe Leu Phe Gly Thr Arg Thr Lys
245                 250                 255

Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser Ser Asp Lys Thr
260                 265                 270

His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser
275                 280                 285

Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg
290                 295                 300

Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro
305                 310                 315                 320

Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala
325                 330                 335

Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val
340                 345                 350

Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr
355                 360                 365

Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr
370                 375                 380

Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu
385                 390                 395                 400

Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys
405                 410                 415

Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser
420                 425                 430

Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp
435                 440                 445

Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser
450                 455                 460

Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala
465                 470                 475                 480

Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
485                 490                 495


<210> SEQ ID NO 194
<211> LENGTH: 1509
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
```

-continued

<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 194

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

caggtgcagc tggtgcagtc tggagctgag gtgaagaagc ctgggtcctc ggtgaaggtc 120

tcctgcaagg cttctggtta cacctttacc agctatggta tcagctgggt gcgacaggcc 180

cctggacaag ggcttgagtg gatgggatgg atcagcgctt acaatggtaa cacaaactat 240

gcacagaagc tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 300

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagtcccg 360

ggcgtaagtg ggagctatcc agactactac tacatggacg tctggggcaa gggaaccctg 420

gtcaccgtct cctcaggtgg aggcggttca ggcggtggca gcggcggtgg cggatcggac 480

atccagatga cccagtctcc ttccaccctg tctgcatcta ttggagacag agtcaccatc 540

acctgccggg ccagtgaggg tatttatcac tggttggcct ggtatcagca gaagccaggg 600

aaagctccta aactcctgat ctataaggcc tctagtttag ccagtggggc cccatcaagg 660

ttcagcggca gtggatctgg gacagatttc actctcacca tcagcagcct gcagcctgat 720

gattttgcaa cttattactg ccaacaatat agtaattatc cgctcacttt cggcggaggg 780

accaagctgg agatcaaacg tgacgtacgc gagcccaaat cttctgacaa aactcacaca 840

tgcccaccgt gcccagcacc tgaactcctg ggtggaccgt cagtcttcct cttccccca 900

aaacccaagg acaccctcat gatctcccgg acccctgagg tcacatgcgt ggtggtggac 960

gtgagccacg aagaccctga ggtcaagttc aactggtacg tggacggcgt ggaggtgcat 1020

aatgccaaga caaagccgcg ggaggagcag tacaacagca cgtaccgtgt ggtcagcgtc 1080

ctcaccgtcc tgcaccagga ctggctgaat ggcaaggagt acaagtgcaa ggtctccaac 1140

aaagccctcc cagccccat cgagaaaacc atctccaaag ccaaagggca gccccgagaa 1200

ccacaggtgt acaccctgcc cccatcccgg gatgagctga ccaagaacca ggtcagcctg 1260

acctgcctgg tcaaaggctt ctatccaagc gacatcgccg tggagtggga gagcaatggg 1320

cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctccttcttc 1380

ctctacagca agctcaccgt ggacaagagc aggtggcagc aggggaacgt cttctcatgc 1440

tccgtgatgc atgaggctct gcacaaccac tacacgcaga agagcctctc cctgtctccg 1500

ggtaaatga 1509

<210> SEQ ID NO 195
<211> LENGTH: 502
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 195

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
20 25 30

Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr

-continued

```
35                  40                  45

Phe Thr Ser Tyr Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly
50                  55                  60

Leu Glu Trp Met Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr
65                  70                  75                  80

Ala Gln Lys Leu Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr
85                  90                  95

Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala
100                 105                 110

Val Tyr Tyr Cys Ala Arg Val Pro Gly Val Ser Gly Ser Tyr Pro Asp
115                 120                 125

Tyr Tyr Tyr Met Asp Val Trp Gly Lys Gly Thr Leu Val Thr Val Ser
130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp
145                 150                 155                 160

Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Ile Gly Asp
165                 170                 175

Arg Val Thr Ile Thr Cys Arg Ala Ser Glu Gly Ile Tyr His Trp Leu
180                 185                 190

Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
195                 200                 205

Lys Ala Ser Ser Leu Ala Ser Gly Ala Pro Ser Arg Phe Ser Gly Ser
210                 215                 220

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp
225                 230                 235                 240

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Asn Tyr Pro Leu Thr
245                 250                 255

Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Asp Val Arg Glu Pro
260                 265                 270

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
275                 280                 285

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
290                 295                 300

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
305                 310                 315                 320

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
325                 330                 335

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
340                 345                 350

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
355                 360                 365

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
370                 375                 380

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
385                 390                 395                 400

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
405                 410                 415

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
420                 425                 430

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
435                 440                 445
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Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
450 455 460

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
465 470 475 480

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
485 490 495

Ser Leu Ser Pro Gly Lys
500

<210> SEQ ID NO 196
<211> LENGTH: 1509
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 196

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 120

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 180

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 240

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 300

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagatggagg 360

cctcttctag actaccactt tgaccaatgg ggccaaggga caatggtcac cgtctcgagt 420

ggaggcggcg gttcaggcgg aggtggctct ggcggtggcg gaagtgcaca gtctgtgctg 480

actcagccac cctcagcgtc tgggaccccc ggacagacgg taacaatctc ttgttctgga 540

agcagctcca acatcggaag tagtgttgtt aattggtacc agcagttccc aggaacggcc 600

cccaaagtcc tcgtctatag taacactcag cggccctcag gggtccctga ccgattctct 660

ggctccaggt ctggcacctc agcctccctg gccatcagtg ggctccagtc tgaggatgag 720

gctgattatt actgtttagc atgggatgcc agcctgaatg gttgggtgtt cggcggaggg 780

accaagctga ccgtcctagg tgacgtacgc gagcccaaat cttctgacaa aactcacaca 840

tgcccaccgt gcccagcacc tgaactcctg ggtggaccgt cagtcttcct cttccccca 900

aaacccaagg acaccctcat gatctcccgg acccctgagg tcacatgcgt ggtggtggac 960

gtgagccacg aagaccctga ggtcaagttc aactggtacg tggacggcgt ggaggtgcat 1020

aatgccaaga caaagccgcg ggaggagcag tacaacagca cgtaccgtgt ggtcagcgtc 1080

ctcaccgtcc tgcaccagga ctggctgaat ggcaaggagt acaagtgcaa ggtctccaac 1140

aaagccctcc cagccccat cgagaaaacc atctccaaag ccaaagggca gccccgagaa 1200

ccacaggtgt acaccctgcc cccatcccgg gatgagctga ccaagaacca ggtcagcctg 1260

acctgcctgg tcaaaggctt ctatccaagc gacatcgccg tggagtggga gagcaatggg 1320

cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctccttcttc 1380

ctctacagca agctcaccgt ggacaagagc aggtggcagc aggggaacgt cttctcatgc 1440

tccgtgatgc atgaggctct gcacaaccac tacacgcaga agagcctctc cctgtctccg 1500

ggtaaatga 1509

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<210> SEQ ID NO 197
<211> LENGTH: 502
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 197

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val
20 25 30

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Arg Trp Arg Pro Leu Leu Asp Tyr His Phe Asp
115 120 125

Gln Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
130 135 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser Val Leu
145 150 155 160

Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln Thr Val Thr Ile
165 170 175

Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Ser Val Val Asn Trp
180 185 190

Tyr Gln Gln Phe Pro Gly Thr Ala Pro Lys Val Leu Val Tyr Ser Asn
195 200 205

Thr Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Arg Ser
210 215 220

Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln Ser Glu Asp Glu
225 230 235 240

Ala Asp Tyr Tyr Cys Leu Ala Trp Asp Ala Ser Leu Asn Gly Trp Val
245 250 255

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro
260 265 270

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
275 280 285

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
290 295 300

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
305 310 315 320

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
325 330 335

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Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
340                 345                 350

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
355                 360                 365

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
370                 375                 380

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
385                 390                 395                 400

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
405                 410                 415

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
420                 425                 430

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
435                 440                 445

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
450                 455                 460

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
465                 470                 475                 480

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
485                 490                 495

Ser Leu Ser Pro Gly Lys
500
```

<210> SEQ ID NO 198
<211> LENGTH: 1509
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 198

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atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

gaggtgcagc tggtggagac tgggggaggc ttggtacagc ctgggggggtc cctgagactc    120

tcctgtgcag cctctggatt caccttcagt agctatggca tgaactgggt ccgccaggct    180

ccagggaagg ggctggagtg ggtttcatac attagtagtt ctggtaatac catattctac    240

gcagactctg tgaagggccg attcaccatc tccagagaca gtgccaagaa ttcagtgtct    300

ctgcagatga acagcctgag agacgaggac acggctgtgt attactgtgc ttcctactac    360

tcctactact acggtatgga cgcctggggc caggggacaa tggtcaccgt ctcgagtgga    420

ggcggcggtt caggcggagg tggctctggc ggtggcggaa gtgcactttc ctatgtgctg    480

actcagccac cctcagcgtc tgggaccccc gggcagaggg tcaccatctc ttgttctgga    540

agcagctcca acatcggaag taatactgta aactggtacc agcagctccc aggaacggcc    600

cccaaactcc tcatctatag taataatcag cggccctcag gggtccctga ccgattctct    660

ggctccaagt ctggcacctc agcctccctg gccatcagtg ggctgcggtc cgaggatgag    720

gctgattatt actgtgcagc atgggattac agcctgagtg gttgggtgtt cggcggaggg    780

accaaggtca ccgtcctagg tgacgtacgc gagcccaaat cttctgacaa aactcacaca    840

tgcccaccgt gcccagcacc tgaactcctg ggtggaccgt cagtcttcct cttcccccca    900

aaacccaagg acaccctcat gatctcccgg acccctgagg tcacatgcgt ggtggtggac    960
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gtgagccacg aagaccctga ggtcaagttc aactggtacg tggacggcgt ggaggtgcat 1020

aatgccaaga caaagccgcg ggaggagcag tacaacagca cgtaccgtgt ggtcagcgtc 1080

ctcaccgtcc tgcaccagga ctggctgaat ggcaaggagt acaagtgcaa ggtctccaac 1140

aaagccctcc cagccccat cgagaaaacc atctccaaag ccaaagggca gccccgagaa 1200

ccacaggtgt acaccctgcc cccatcccgg gatgagctga ccaagaacca ggtcagcctg 1260

acctgcctgg tcaaaggctt ctatccaagc gacatcgccg tggagtggga gagcaatggg 1320

cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctccttcttc 1380

ctctacagca agctcaccgt ggacaagagc aggtggcagc aggggaacgt cttctcatgc 1440

tccgtgatgc atgaggctct gcacaaccac tacacgcaga agagcctctc cctgtctccg 1500

ggtaaatga 1509

<210> SEQ ID NO 199
<211> LENGTH: 502
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 199

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Val Glu Thr Gly Gly Gly Leu Val
20 25 30

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Ser Tyr Gly Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ser Tyr Ile Ser Ser Ser Gly Asn Thr Ile Phe Tyr
65 70 75 80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Ser Ala Lys
85 90 95

Asn Ser Val Ser Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Ser Tyr Tyr Ser Tyr Tyr Tyr Gly Met Asp Ala
115 120 125

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Leu Ser Tyr Val Leu
145 150 155 160

Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln Arg Val Thr Ile
165 170 175

Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val Asn Trp
180 185 190

Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Ser Asn
195 200 205

Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Lys Ser
210 215 220

Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg Ser Glu Asp Glu

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225 230 235 240

Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Tyr Ser Leu Ser Gly Trp Val
245 250 255

Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Asp Val Arg Glu Pro
260 265 270

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
275 280 285

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
290 295 300

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
305 310 315 320

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
325 330 335

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
340 345 350

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
355 360 365

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
370 375 380

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
385 390 395 400

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
405 410 415

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
420 425 430

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
435 440 445

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
450 455 460

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
465 470 475 480

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
485 490 495

Ser Leu Ser Pro Gly Lys
500

<210> SEQ ID NO 200
<211> LENGTH: 1497
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 200

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtgcagc tggtggagac tggggaaggc ctggtcaagc ctgggggtc cctgagactc 120

tcctgtacag cctctggatt caccttcagg agttatagct tgaactgggt ccgccaggct 180

ccagggcagg ggctggagtg ggtctcatcc attagtagta ctagtactta catatactac 240

gcagactcgg tgaagggccg attcaccatc tccagagacg acgccaagaa cacactgtat 300

ctgcaaatga acagcctgag agccgaagac acagctgcat attactgtgt tagactggga 360

-continued

tctggtgggg gatattttcc tgactactgg ggcaggggca ccctggtcac cgtctcgagt 420

ggtggaggcg gttcaggcgg aggtggcagc ggcggtggcg gatcgtctga gctgactcag 480

gaccctgctg tgtctgtggc cttgggacag acagtcagga tcacatgcca aggagacagc 540

ctcagaagct attatgcaag ctggtaccag cagaagccag gacaggcccc tgtacttgtc 600

atctatggta aaaacaaccg gccctcaggg atcccagacc gattctctgg ctccagctca 660

ggaaacacag cttccttgac catcactggg gctcaggcgg aagatgaggc tgactattac 720

tgtaactccc gggacagcag tggtaaccat gtggtattcg gcggagggac caagctgacc 780

gtcctaggtg acgtacgcga gcccaaatct tctgacaaaa ctcacacatg cccaccgtgc 840

ccagcacctg aactcctggg tggaccgtca gtcttcctct tccccccaaa acccaaggac 900

accctcatga tctcccggac ccctgaggtc acatgcgtgg tggtggacgt gagccacgaa 960

gaccctgagg tcaagttcaa ctggtacgtg gacggcgtgg aggtgcataa tgccaagaca 1020

aagccgcggg aggagcagta caacagcacg taccgtgtgg tcagcgtcct caccgtcctg 1080

caccaggact ggctgaatgg caaggagtac aagtgcaagg tctccaacaa agccctccca 1140

gcccccatcg agaaaaccat ctccaaagcc aaagggcagc cccgagaacc acaggtgtac 1200

accctgcccc catcccggga tgagctgacc aagaaccagg tcagcctgac ctgcctggtc 1260

aaaggcttct atccaagcga catcgccgtg gagtgggaga gcaatgggca gccggagaac 1320

aactacaaga ccacgcctcc cgtgctggac tccgacggct ccttcttcct ctacagcaag 1380

ctcaccgtgg acaagagcag gtggcagcag gggaacgtct tctcatgctc cgtgatgcat 1440

gaggctctgc acaaccacta cacgcagaag agcctctccc tgtctccggg taaatga 1497

<210> SEQ ID NO 201
<211> LENGTH: 498
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 201

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Val Glu Thr Gly Glu Gly Leu Val
20 25 30

Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Thr Ala Ser Gly Phe Thr
35 40 45

Phe Arg Ser Tyr Ser Leu Asn Trp Val Arg Gln Ala Pro Gly Gln Gly
50 55 60

Leu Glu Trp Val Ser Ser Ile Ser Ser Thr Ser Thr Tyr Ile Tyr Tyr
65 70 75 80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ala Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100 105 110

Ala Tyr Tyr Cys Val Arg Leu Gly Ser Gly Gly Gly Tyr Phe Pro Asp
115 120 125

Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly

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130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Glu Leu Thr Gln
145                 150                 155                 160

Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val Arg Ile Thr Cys
165                 170                 175

Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser Trp Tyr Gln Gln Lys
180                 185                 190

Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Lys Asn Asn Arg Pro
195                 200                 205

Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Asn Thr Ala
210                 215                 220

Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp Tyr Tyr
225                 230                 235                 240

Cys Asn Ser Arg Asp Ser Ser Gly Asn His Val Val Phe Gly Gly Gly
245                 250                 255

Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser Ser Asp
260                 265                 270

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
275                 280                 285

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
290                 295                 300

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
305                 310                 315                 320

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
325                 330                 335

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
340                 345                 350

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
355                 360                 365

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
370                 375                 380

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr
385                 390                 395                 400

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
405                 410                 415

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
420                 425                 430

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
435                 440                 445

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
450                 455                 460

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
465                 470                 475                 480

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
485                 490                 495

Gly Lys


<210> SEQ ID NO 202
<211> LENGTH: 1509
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
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<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 202

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

caggtgcagc tggtggagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtc 120

tcctgcaagg cttctggata caccttcacc agttatgata tcaactgggt gcgacaggcc 180

cccggacaaa ggcttgagtg gatgggatgg atcaacgctg gcaatggtaa cacaaaatat 240

tcacagaagt tccagggcag agtcaccatt accagggaca catccgcgag cacagcctac 300

atggagctga ggagcctgag atctgacgac acggccgtgt attactgtgc gagagggagg 360

agctatggcc acccgtacta ctttgactac tggggccagg gaaccctggt caccgtctcg 420

agtggtggag gcggttcagg cggaggtggc agcggcggtg gcggatcgca gtctgtgctg 480

actcagcctg cctccgtgtc tgggtctcct ggacagtcga tcaccatctc ctgcactgga 540

accagcagtg acgttggtgg ttataactat gtctcctggt accaacaaca cccaggcaaa 600

gcccccaaac tcatgattta tgagggcagt aagcggccct caggggtttc taatcgcttc 660

tctggctcca agtctggcaa cacggcctcc ctgacaatct ctgggctcca ggctgaggac 720

gaggctgatt attactgcag ctcatataca accaggagca ctcgagtttt cggcggaggg 780

accaagctga ccgtcctagg tgacgtacgc gagcccaaat cttctgacaa aactcacaca 840

tgcccaccgt gcccagcacc tgaactcctg ggtggaccgt cagtcttcct cttccccca 900

aaacccaagg acaccctcat gatctcccgg acccctgagg tcacatgcgt ggtggtggac 960

gtgagccacg aagaccctga ggtcaagttc aactggtacg tggacggcgt ggaggtgcat 1020

aatgccaaga caaagccgcg ggaggagcag tacaacagca cgtaccgtgt ggtcagcgtc 1080

ctcaccgtcc tgcaccagga ctggctgaat ggcaaggagt acaagtgcaa ggtctccaac 1140

aaagccctcc cagccccat cgagaaaacc atctccaaag ccaaagggca gccccgagaa 1200

ccacaggtgt acaccctgcc cccatcccgg gatgagctga ccaagaacca ggtcagcctg 1260

acctgcctgg tcaaaggctt ctatccaagc gacatcgccg tggagtggga gagcaatggg 1320

cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctccttcttc 1380

ctctacagca agctcaccgt ggacaagagc aggtggcagc aggggaacgt cttctcatgc 1440

tccgtgatgc atgaggctct gcacaaccac tacacgcaga agagcctctc cctgtctccg 1500

ggtaaatga 1509

<210> SEQ ID NO 203
<211> LENGTH: 502
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 203

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Gln Val Gln Leu Val Glu Ser Gly Ala Glu Val Lys
20 25 30

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Lys Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr
35                  40                  45

Phe Thr Ser Tyr Asp Ile Asn Trp Val Arg Gln Ala Pro Gly Gln Arg
50                  55                  60

Leu Glu Trp Met Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr
65                  70                  75                  80

Ser Gln Lys Phe Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala
85                  90                  95

Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala
100                 105                 110

Val Tyr Tyr Cys Ala Arg Gly Arg Ser Tyr Gly His Pro Tyr Tyr Phe
115                 120                 125

Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130                 135                 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Val Leu
145                 150                 155                 160

Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile
165                 170                 175

Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser
180                 185                 190

Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu
195                 200                 205

Gly Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys
210                 215                 220

Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp
225                 230                 235                 240

Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg Ser Thr Arg Val
245                 250                 255

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro
260                 265                 270

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
275                 280                 285

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
290                 295                 300

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
305                 310                 315                 320

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
325                 330                 335

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
340                 345                 350

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
355                 360                 365

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
370                 375                 380

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
385                 390                 395                 400

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
405                 410                 415

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
420                 425                 430

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
```

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435 440 445

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
450 455 460

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
465 470 475 480

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
485 490 495

Ser Leu Ser Pro Gly Lys
500

<210> SEQ ID NO 204
<211> LENGTH: 1518
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence: Syntheticpolynucleotide"

<400> SEQUENCE: 204

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

aaggtgcagc tggtgcagtc tgggacagag gtgaaaaagc ccggggagtc tctgaagatc 120

tcctgtcagg gttctggata caggtttagt agtgactgga ttgcctgggt gcgccagatg 180

cccgggaaag gcctggagtg gatggggatt gtctatcctg gtgactctga taccagatat 240

agcccgtcct tccaaggcca agtcaccatc tcagccgaca agtccatcag tactgcctac 300

ctgcagtgga gcggcctgaa ggcctcggac accgccaagt attactgtgc gagagtgcaa 360

caggcagtgg gagctaaagg ttatgctatg gacgtctggg gcaagggaac cctggtcacc 420

gtctcgagtg gaggcggcgg ttcaggcgga ggtggctctg gcggtggcgg aagtgcacag 480

actgtggtga tccaggagcc atcgttctca gtgtcccctg gagggacagt cacactcact 540

tgtggcttga gctctggctc agtctctacc agttactacc ccagctggta ccggcagacc 600

ccaggccagg ctccacacac actcattcac aacacaaaga ttcgctcctc tggggtccct 660

gatcgcttct ctggctccat ccttgggaac aatgctgccc tcaccatcac gggggcccag 720

gcagatgatg aatctgatta ttactgtctt ttgtatatgg gtagcggcat ttacgtgttc 780

ggcggaggga ccaagctgac cgtcctaggt gacgtacgcg agcccaaatc ttctgacaaa 840

actcacacat gcccaccgtg cccagcacct gaactcctgg gtggaccgtc agtcttcctc 900

ttccccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg 960

gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt ggacggcgtg 1020

gaggtgcata atgccaagac aaagccgcgg gaggagcagt acaacagcac gtaccgtgtg 1080

gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag 1140

gtctccaaca aagccctccc agccccccatc gagaaaacca tctccaaagc caaagggcag 1200

ccccgagaac cacaggtgta caccctgccc ccatcccggg atgagctgac caagaaccag 1260

gtcagcctga cctgcctggt caaaggcttc tatccaagcg acatcgccgt ggagtgggag 1320

agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga ctccgacggc 1380

tccttcttcc tctacagcaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc 1440

ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc 1500

-continued

ctgtctccgg gtaaatga 1518

<210> SEQ ID NO 205
<211> LENGTH: 505
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 205

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Lys Val Gln Leu Val Gln Ser Gly Thr Glu Val Lys
20 25 30

Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Gln Gly Ser Gly Tyr Arg
35 40 45

Phe Ser Ser Asp Trp Ile Ala Trp Val Arg Gln Met Pro Gly Lys Gly
50 55 60

Leu Glu Trp Met Gly Ile Val Tyr Pro Gly Asp Ser Asp Thr Arg Tyr
65 70 75 80

Ser Pro Ser Phe Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile
85 90 95

Ser Thr Ala Tyr Leu Gln Trp Ser Gly Leu Lys Ala Ser Asp Thr Ala
100 105 110

Lys Tyr Tyr Cys Ala Arg Val Gln Gln Ala Val Gly Ala Lys Gly Tyr
115 120 125

Ala Met Asp Val Trp Gly Lys Gly Thr Leu Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln
145 150 155 160

Thr Val Val Ile Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly Thr
165 170 175

Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser Tyr
180 185 190

Tyr Pro Ser Trp Tyr Arg Gln Thr Pro Gly Gln Ala Pro His Thr Leu
195 200 205

Ile His Asn Thr Lys Ile Arg Ser Ser Gly Val Pro Asp Arg Phe Ser
210 215 220

Gly Ser Ile Leu Gly Asn Asn Ala Ala Leu Thr Ile Thr Gly Ala Gln
225 230 235 240

Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Leu Leu Tyr Met Gly Ser Gly
245 250 255

Ile Tyr Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val
260 265 270

Arg Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro
275 280 285

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
290 295 300

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
305 310 315 320

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
325 330 335

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```
Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
340                 345                 350

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
355                 360                 365

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
370                 375                 380

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
385                 390                 395                 400

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
405                 410                 415

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
420                 425                 430

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
435                 440                 445

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
450                 455                 460

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
465                 470                 475                 480

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
485                 490                 495

Lys Ser Leu Ser Leu Ser Pro Gly Lys
500                 505


<210> SEQ ID NO 206
<211> LENGTH: 1518
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolynucleotide"

<400> SEQUENCE: 206

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

gaagtgcagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgagggtc    120

tcctgcaagg gttctggaaa caccttcacc ggccactaca tccactgggt gcgacaggcc    180

cctggacaag gacttgagtg gctgggatgg atcgacccta acactggtga catacagtat    240

tcagaaaact ttaagggctc ggtcaccttg accagggacc atccatcaa ctcagtcttc    300

atggacctga tcaggctgac atctgacgac acggccatgt attactgtgc gagagaaggt    360

gccgggctcg ccaactacta ttactacggt ctggacgtct ggggccgagg gacaatggtc    420

accgtctcga gtggaggcgg cggttcaggc ggaggtggct ctggcggtgg cggaagtgca    480

cagactgtgg tgctccagga gccttcgttc tcagtgtccc ctgggggggac agtcacactc    540

acttgtggct tgaactttgg ctcagtctct actgcttact accccagttg gtaccagcag    600

accccaggcc aagctccacg cacgctcatc tacggcacaa atattcgttc ctctggggtc    660

ccggatcgct tctctggctc catcgtaggg aacaaagctg ccctcaccat cacgggggcc    720

cagacagaag atgagtctga ttattattgt gcgctgtata tgggtagtgg catgctcttc    780

ggcggcggga ccaaggtcac cgtcctaggt gacgtacgcg agcccaaatc ttctgacaaa    840

actcacacat gcccaccgtg cccagcacct gaactcctgg gtggaccgtc agtcttcctc    900
```

-continued

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ttccccccaa aacccaagga caccctcatg atctcccgga cccctgaggt cacatgcgtg    960

gtggtggacg tgagccacga agaccctgag gtcaagttca actggtacgt ggacggcgtg   1020

gaggtgcata atgccaagac aaagccgcgg gaggagcagt acaacagcac gtaccgtgtg   1080

gtcagcgtcc tcaccgtcct gcaccaggac tggctgaatg gcaaggagta caagtgcaag   1140

gtctccaaca aagccctccc agccccccatc gagaaaacca tctccaaagc caaagggcag   1200

ccccgagaac cacaggtgta caccctgccc ccatcccggg atgagctgac caagaaccag   1260

gtcagcctga cctgcctggt caaaggcttc tatccaagcg acatcgccgt ggagtgggag   1320

agcaatgggc agccggagaa caactacaag accacgcctc ccgtgctgga ctccgacggc   1380

tccttcttcc tctacagcaa gctcaccgtg gacaagagca ggtggcagca ggggaacgtc   1440

ttctcatgct ccgtgatgca tgaggctctg cacaaccact acacgcagaa gagcctctcc   1500

ctgtctccgg gtaaatga                                                 1518
```

<210> SEQ ID NO 207
<211> LENGTH: 505
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 207

```
Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1               5                   10                  15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
20                  25                  30

Lys Pro Gly Ala Ser Val Arg Val Ser Cys Lys Gly Ser Gly Asn Thr
35                  40                  45

Phe Thr Gly His Tyr Ile His Trp Val Arg Gln Ala Pro Gly Gln Gly
50                  55                  60

Leu Glu Trp Leu Gly Trp Ile Asp Pro Asn Thr Gly Asp Ile Gln Tyr
65                  70                  75                  80

Ser Glu Asn Phe Lys Gly Ser Val Thr Leu Thr Arg Asp Pro Ser Ile
85                  90                  95

Asn Ser Val Phe Met Asp Leu Ile Arg Leu Thr Ser Asp Asp Thr Ala
100                 105                 110

Met Tyr Tyr Cys Ala Arg Glu Gly Ala Gly Leu Ala Asn Tyr Tyr Tyr
115                 120                 125

Tyr Gly Leu Asp Val Trp Gly Arg Gly Thr Met Val Thr Val Ser Ser
130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala
145                 150                 155                 160

Gln Thr Val Val Leu Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
165                 170                 175

Thr Val Thr Leu Thr Cys Gly Leu Asn Phe Gly Ser Val Ser Thr Ala
180                 185                 190

Tyr Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
195                 200                 205

Leu Ile Tyr Gly Thr Asn Ile Arg Ser Ser Gly Val Pro Asp Arg Phe
210                 215                 220
```

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```
Ser Gly Ser Ile Val Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
225                 230                 235                 240

Gln Thr Glu Asp Glu Ser Asp Tyr Tyr Cys Ala Leu Tyr Met Gly Ser
245                 250                 255

Gly Met Leu Phe Gly Gly Gly Thr Lys Val Thr Val Leu Gly Asp Val
260                 265                 270

Arg Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro
275                 280                 285

Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys
290                 295                 300

Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val
305                 310                 315                 320

Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr
325                 330                 335

Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu
340                 345                 350

Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His
355                 360                 365

Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys
370                 375                 380

Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln
385                 390                 395                 400

Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu
405                 410                 415

Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro
420                 425                 430

Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn
435                 440                 445

Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu
450                 455                 460

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val
465                 470                 475                 480

Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln
485                 490                 495

Lys Ser Leu Ser Leu Ser Pro Gly Lys
500                 505
```

<210> SEQ ID NO 208
<211> LENGTH: 1503
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 208

```
atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

gaagtgcagc tggtgcagtc tggggctgaa gtgaagaagc ctggggcctc agtgaaggtc    120

tcttgtcagg cttctggata caccttcagc gggcactata tgcacttggt gcgacaggcc    180

cctggacaag ggcttgagtg gatggggtgg atccacccta ccagtggtgg cacaacctat    240

gcacagaagt ttcagggccg ggtcgttatg accagggaca cgtccatcag cacagcctac    300
```

-continued

atggaactga gtaggctgac atctgacgac acggccgtgt attactgtgc aagaatgtcc 360

caaaactatg atgcttttga tatctggggc caagggacaa tggtcaccgt ctcgagtgga 420

ggcggcggtt caggcggagg tggctctggc ggtggcggaa gtgcacaggc tgtgctgact 480

cagccgtcct cagtgtctgg ggccccaggg cagagggtca ccatctcctg cactgggagc 540

agctccaaca tcggggcagg ttatgatgta aactggtacc aacaatttcc aggaacagcc 600

cccaaaatta tcgtctatgg cgatcggccc tcaggggccc ctgaccgatt ctctggctcc 660

aagtctggca cctcagcctc cctggcaatc actggactcc gggctgagga tgaggctgat 720

tattactgcc agtcctggga cagtcgcctg agtagttatg tcttcggaac tgggaccaag 780

gtcaccgtcc taggtgacgt acgcgagccc aaatcttctg acaaaactca cacatgccca 840

ccgtgcccag cacctgaact cctgggtgga ccgtcagtct tcctcttccc cccaaaaccc 900

aaggacaccc tcatgatctc ccggacccct gaggtcacat gcgtggtggt ggacgtgagc 960

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 1020

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 1080

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 1140

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 1200

gtgtacaccc tgccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc 1260

ctggtcaaag gcttctatcc aagcgacatc gccgtggagt gggagagcaa tgggcagccg 1320

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 1380

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 1440

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 1500

tga 1503

<210> SEQ ID NO 209
<211> LENGTH: 500
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 209

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
20 25 30

Lys Pro Gly Ala Ser Val Lys Val Ser Cys Gln Ala Ser Gly Tyr Thr
35 40 45

Phe Ser Gly His Tyr Met His Leu Val Arg Gln Ala Pro Gly Gln Gly
50 55 60

Leu Glu Trp Met Gly Trp Ile His Pro Thr Ser Gly Gly Thr Thr Tyr
65 70 75 80

Ala Gln Lys Phe Gln Gly Arg Val Val Met Thr Arg Asp Thr Ser Ile
85 90 95

Ser Thr Ala Tyr Met Glu Leu Ser Arg Leu Thr Ser Asp Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Arg Met Ser Gln Asn Tyr Asp Ala Phe Asp Ile

-continued

```
115                 120                 125

Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser
130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ala Val Leu Thr
145                 150                 155                 160

Gln Pro Ser Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser
165                 170                 175

Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Tyr Asp Val Asn Trp
180                 185                 190

Tyr Gln Gln Phe Pro Gly Thr Ala Pro Lys Ile Ile Val Tyr Gly Asp
195                 200                 205

Arg Pro Ser Gly Ala Pro Asp Arg Phe Ser Gly Ser Lys Ser Gly Thr
210                 215                 220

Ser Ala Ser Leu Ala Ile Thr Gly Leu Arg Ala Glu Asp Glu Ala Asp
225                 230                 235                 240

Tyr Tyr Cys Gln Ser Trp Asp Ser Arg Leu Ser Ser Tyr Val Phe Gly
245                 250                 255

Thr Gly Thr Lys Val Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser
260                 265                 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
275                 280                 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385                 390                 395                 400

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
405                 410                 415

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
485                 490                 495

Ser Pro Gly Lys
500
```

<210> SEQ ID NO 210

-continued

<211> LENGTH: 1533
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 210

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtgcagc tggtgcagtc tggggcagag gtgaaaaagc ccggagagtc tctgaagatc 120

tcctgtaagg gctctggata cacctttacc aaccactgga tcgcctgggt gcgccagatg 180

cccgggaaag gcctggagtg gatgggcatc atctatcctg gtgactctga aacgaggtac 240

agcccgtcct tccaaggcca cgtcaccatc tcagccgaca agtccatcag taccgcctat 300

ttgcagtgga gcaccctgaa ggactcggac tccgccatgt acttctgtgt gagacaggcc 360

cgtggctggg acgacggacg ggctggatat tattattccg gtatggacgc ctggggccag 420

ggaaccctgg tcaccgtctc gagtggaggc ggcggttcag gcggaggtgg ctctggcggt 480

ggcggaagtg cacaggctgt ggtgctccag gagccatcgt tctcagtgtc ccctggaggg 540

acagtcacac tcacctgtgg cttgcgctct gggtcagtct ctactagtca ctaccccagc 600

tggtaccagc agaccccagg ccaggctcca cgcacgctca tttacagcac aaacactcgc 660

tcttctgggg tccctgatcg cttctctggc tccatccttg ggaacaaagc tgccctcacc 720

atcacggggg cccaggcaga tgatgaatct aattattact gtatgctata catgggcagt 780

ggcatgtatg tgttcggcgg agggaccaag gtcaccgtcc taggtgacgt acgcgagccc 840

aaatcttctg acaaaactca cacatgccca ccgtgcccag cacctgaact cctgggtgga 900

ccgtcagtct tcctcttccc cccaaaaccc aaggacaccc tcatgatctc ccggaccccct 960

gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 1020

tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac 1080

agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 1140

gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 1200

aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggatgag 1260

ctgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc aagcgacatc 1320

gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 1380

ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 1440

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg 1500

cagaagagcc tctccctgtc tccgggtaaa tga 1533

<210> SEQ ID NO 211
<211> LENGTH: 510
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 211

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

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```
Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
20                  25                  30

Lys Pro Gly Glu Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Thr
35                  40                  45

Phe Thr Asn His Trp Ile Ala Trp Val Arg Gln Met Pro Gly Lys Gly
50                  55                  60

Leu Glu Trp Met Gly Ile Ile Tyr Pro Gly Asp Ser Glu Thr Arg Tyr
65                  70                  75                  80

Ser Pro Ser Phe Gln Gly His Val Thr Ile Ser Ala Asp Lys Ser Ile
85                  90                  95

Ser Thr Ala Tyr Leu Gln Trp Ser Thr Leu Lys Asp Ser Asp Ser Ala
100                 105                 110

Met Tyr Phe Cys Val Arg Gln Ala Arg Gly Trp Asp Asp Gly Arg Ala
115                 120                 125

Gly Tyr Tyr Tyr Ser Gly Met Asp Ala Trp Gly Gln Gly Thr Leu Val
130                 135                 140

Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
145                 150                 155                 160

Gly Gly Ser Ala Gln Ala Val Val Leu Gln Glu Pro Ser Phe Ser Val
165                 170                 175

Ser Pro Gly Gly Thr Val Thr Leu Thr Cys Gly Leu Arg Ser Gly Ser
180                 185                 190

Val Ser Thr Ser His Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln
195                 200                 205

Ala Pro Arg Thr Leu Ile Tyr Ser Thr Asn Thr Arg Ser Ser Gly Val
210                 215                 220

Pro Asp Arg Phe Ser Gly Ser Ile Leu Gly Asn Lys Ala Ala Leu Thr
225                 230                 235                 240

Ile Thr Gly Ala Gln Ala Asp Asp Glu Ser Asn Tyr Tyr Cys Met Leu
245                 250                 255

Tyr Met Gly Ser Gly Met Tyr Val Phe Gly Gly Gly Thr Lys Val Thr
260                 265                 270

Val Leu Gly Asp Val Arg Glu Pro Lys Ser Ser Asp Lys Thr His Thr
275                 280                 285

Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe
290                 295                 300

Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro
305                 310                 315                 320

Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val
325                 330                 335

Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr
340                 345                 350

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val
355                 360                 365

Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys
370                 375                 380

Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser
385                 390                 395                 400

Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro
405                 410                 415
```

-continued

```
Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val
420                 425                 430

Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly
435                 440                 445

Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp
450                 455                 460

Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp
465                 470                 475                 480

Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His
485                 490                 495

Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
500                 505                 510


<210> SEQ ID NO 212
<211> LENGTH: 1527
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolynucleotide"

<400> SEQUENCE: 212

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc    120

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct    180

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac    240

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat    300

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagatctg    360

ggaatagacc ccctttggag tggttattac acacccccttg actattgggg ccgagggaca    420

atggtcaccg tctcgagtgg aggcggcggt tcaggcggag gtggctctgg cggtggcgga    480

agtgcacacg ttatactgac tcaaccgccc tcagcgtctg ggacccccgg gcagagggtc    540

accatctctt gttctggaag cagctccaac atcggaagta attccgttag ctggtaccag    600

cagctcccag gaacggcccc caaactcctc atgtatacta acaatcagcg gccctcaggg    660

gtccctgacc gattctctgg ctccaagtct ggcacctcag cctccctggc catcagtggg    720

ctccagtctg aggatgaggc tgattattac tgtgcgacat gggatgccag cctgaatact    780

tgggtgttcg gcggagggac caaggtcacc gtcctaggtg acgtacgcga gcccaaatct    840

tctgacaaaa ctcacacatg cccaccgtgc ccagcacctg aactcctggg tggaccgtca    900

gtcttcctct tccccccaaa acccaaggac accctcatga tctcccggac ccctgaggtc    960

acatgcgtgg tggtggacgt gagccacgaa gaccctgagg tcaagttcaa ctggtacgtg   1020

gacggcgtgg aggtgcataa tgccaagaca aagccgcggg aggagcagta caacagcacg   1080

taccgtgtgg tcagcgtcct caccgtcctg caccaggact ggctgaatgg caaggagtac   1140

aagtgcaagg tctccaacaa agccctccca gcccccatcg agaaaaccat ctccaaagcc   1200

aaagggcagc cccgagaacc acaggtgtac accctgcccc catcccggga tgagctgacc   1260

aagaaccagg tcagcctgac ctgcctggtc aaaggcttct atccaagcga catcgccgtg   1320

gagtgggaga gcaatgggca gccggagaac aactacaaga ccacgcctcc cgtgctggac   1380
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tccgacggct ccttcttcct ctacagcaag ctcaccgtgg acaagagcag gtggcagcag 1440

gggaacgtct tctcatgctc cgtgatgcat gaggctctgc acaaccacta cacgcagaag 1500

agcctctccc tgtctccggg taaatga 1527

<210> SEQ ID NO 213
<211> LENGTH: 508
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 213

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val
20 25 30

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Arg Asp Leu Gly Ile Asp Pro Leu Trp Ser Gly
115 120 125

Tyr Tyr Thr Pro Leu Asp Tyr Trp Gly Arg Gly Thr Met Val Thr Val
130 135 140

Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
145 150 155 160

Ser Ala His Val Ile Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro
165 170 175

Gly Gln Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly
180 185 190

Ser Asn Ser Val Ser Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys
195 200 205

Leu Leu Met Tyr Thr Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg
210 215 220

Phe Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly
225 230 235 240

Leu Gln Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Thr Trp Asp Ala
245 250 255

Ser Leu Asn Thr Trp Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
260 265 270

Gly Asp Val Arg Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro
275 280 285

Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe
290 295 300

Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val

-continued

305 310 315 320

Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe
325 330 335

Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro
340 345 350

Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr
355 360 365

Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val
370 375 380

Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala
385 390 395 400

Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg
405 410 415

Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly
420 425 430

Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro
435 440 445

Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser
450 455 460

Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln
465 470 475 480

Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His
485 490 495

Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
500 505

<210> SEQ ID NO 214
<211> LENGTH: 1506
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 214

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtccagc tggtgcagtc tggagctgag gtgaaggagc ctggggcctc agtgaaggtc 120

tcctgcaagg cctctggtta cgacttttcc aactatggtt tcagctgggt gcgccaggcc 180

cctggacaag gtcttgagtg gatgggatgg atcagctctt ataatggtta cacaaactat 240

gcacagagac tccagggcag agtcaccatg accacagaca catccacgag cacagcctac 300

atggagctga ggagcctgag atctgacgac acagctgtct attactgtgc gagagatcga 360

ggacttggaa actggtactt cgatctctgg ggccaaggca ccctggtcac cgtctcgagt 420

ggtggaggcg gttcaggcgg aggtggcagc ggcggtggcg gatcgcagtc tgtgctgact 480

cagcctgcct ccgtgtctgg gtctcctgga cagtcgatca ccatctcctg cactggaacc 540

agcagtgacg ttggtggtta taactatgtc tcctggtacc aacaacaccc aggcaaagcc 600

cccaaactca tgatttatga gggcagtaag cggccctcag gggtttctaa tcgcttctct 660

ggctccaagt ctggcaacac ggcctccctg acaatctctg ggctccaggc tgaggacgag 720

gctgattatt actgcagctc atatacaacc aggagcactc gagttttcgg cggagggacc 780

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aagctgaccg tcctaggtga cgtacgcgag cccaaatctt ctgacaaaac tcacacatgc    840

ccaccgtgcc cagcacctga actcctgggt ggaccgtcag tcttcctctt ccccccaaaa    900

cccaaggaca ccctcatgat ctcccggacc cctgaggtca catgcgtggt ggtggacgtg    960

agccacgaag accctgaggt caagttcaac tggtacgtgg acggcgtgga ggtgcataat   1020

gccaagacaa agccgcggga ggagcagtac aacagcacgt accgtgtggt cagcgtcctc   1080

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa   1140

gccctcccag cccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca   1200

caggtgtaca ccctgccccc atcccgggat gagctgacca agaaccaggt cagcctgacc   1260

tgcctggtca aaggcttcta tccaagcgac atcgccgtgg agtgggagag caatgggcag   1320

ccggagaaca actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc   1380

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc   1440

gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctccgggt   1500

aaatga                                                              1506
```

<210> SEQ ID NO 215
<211> LENGTH: 501
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 215

```
Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1               5                   10                  15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys
20                  25                  30

Glu Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Asp
35                  40                  45

Phe Ser Asn Tyr Gly Phe Ser Trp Val Arg Gln Ala Pro Gly Gln Gly
50                  55                  60

Leu Glu Trp Met Gly Trp Ile Ser Ser Tyr Asn Gly Tyr Thr Asn Tyr
65                  70                  75                  80

Ala Gln Arg Leu Gln Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr
85                  90                  95

Ser Thr Ala Tyr Met Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala
100                 105                 110

Val Tyr Tyr Cys Ala Arg Asp Arg Gly Leu Gly Asn Trp Tyr Phe Asp
115                 120                 125

Leu Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly
130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr
145                 150                 155                 160

Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser
165                 170                 175

Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp
180                 185                 190

Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu Met Ile Tyr Glu Gly
195                 200                 205
```

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Ser Lys Arg Pro Ser Gly Val Ser Asn Arg Phe Ser Gly Ser Lys Ser
210                 215                 220

Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu
225                 230                 235                 240

Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr Thr Arg Ser Thr Arg Val Phe
245                 250                 255

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys
260                 265                 270

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
275                 280                 285

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
290                 295                 300

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
305                 310                 315                 320

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
325                 330                 335

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
340                 345                 350

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
355                 360                 365

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
370                 375                 380

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
385                 390                 395                 400

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
405                 410                 415

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
420                 425                 430

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
435                 440                 445

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
450                 455                 460

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
465                 470                 475                 480

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
485                 490                 495

Leu Ser Pro Gly Lys
500


<210> SEQ ID NO 216
<211> LENGTH: 1509
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolynucleotide"

<400> SEQUENCE: 216

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

cagatgcagc tggtgcagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc    120

tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct    180
```

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ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtat taaatactat    240

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacactgtat    300

ctacaaatga acagcctgag agccgaggac acgggcgttt attactgttc gaaagatcgc    360

tatagcagtg gctggtacag ctccgatgct tttgatattt ggggccgagg gacaatggtc    420

accgtctcga gtggtggagg cggttcaggc ggaggtggca gcggcggtgg cggatcgtct    480

gagctgactc aggaccctgc tgtgtctgtg gccttgggac agacagtcag gatcacatgc    540

caaggagaca gcctcagaag ctattatgca agctggtacc agcagaagcc aggacaggcc    600

cctgtacttg tcatctatgg taaaaacaac cggccctcag ggatcccaga ccgattctct    660

ggctccagct caggaaacac agcttccttg accatcactg gggctcaggc ggaagatgag    720

gctgactatt actgtcattc ccgggacagc agtggtaacc atgtgctttt cggcggaggg    780

accaagctga ccgtcctagg tgacgtacgc gagcccaaat cttctgacaa aactcacaca    840

tgcccaccgt gcccagcacc tgaactcctg ggtggaccgt cagtcttcct cttccccca     900

aaacccaagg acaccctcat gatctcccgg acccctgagg tcacatgcgt ggtggtggac    960

gtgagccacg aagaccctga ggtcaagttc aactggtacg tggacggcgt ggaggtgcat   1020

aatgccaaga caaagccgcg ggaggagcag tacaacagca cgtaccgtgt ggtcagcgtc   1080

ctcaccgtcc tgcaccagga ctggctgaat ggcaaggagt acaagtgcaa ggtctccaac   1140

aaagccctcc cagccccat cgagaaaacc atctccaaag ccaaagggca gccccgagaa    1200

ccacaggtgt acaccctgcc cccatcccgg gatgagctga ccaagaacca ggtcagcctg   1260

acctgcctgg tcaaaggctt ctatccaagc gacatcgccg tggagtggga gagcaatggg   1320

cagccggaga acaactacaa gaccacgcct cccgtgctgg actccgacgg ctccttcttc   1380

ctctacagca agctcaccgt ggacaagagc aggtggcagc aggggaacgt cttctcatgc   1440

tccgtgatgc atgaggctct gcacaaccac tacacgcaga agagcctctc cctgtctccg   1500

ggtaaatga                                                           1509
```

```
<210> SEQ ID NO 217
<211> LENGTH: 502
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 217

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1               5                  10                  15

Asp Thr Thr Gly Gln Met Gln Leu Val Gln Ser Gly Gly Gly Val Val
20                  25                  30

Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35                  40                  45

Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
50                  55                  60

Leu Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Ile Lys Tyr Tyr
65                  70                  75                  80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85                  90                  95
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Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Gly
100                 105                 110

Val Tyr Tyr Cys Ser Lys Asp Arg Tyr Ser Ser Gly Trp Tyr Ser Ser
115                 120                 125

Asp Ala Phe Asp Ile Trp Gly Arg Gly Thr Met Val Thr Val Ser Ser
130                 135                 140

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser
145                 150                 155                 160

Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val
165                 170                 175

Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser Trp
180                 185                 190

Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Lys
195                 200                 205

Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser
210                 215                 220

Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu
225                 230                 235                 240

Ala Asp Tyr Tyr Cys His Ser Arg Asp Ser Ser Gly Asn His Val Leu
245                 250                 255

Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro
260                 265                 270

Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu
275                 280                 285

Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp
290                 295                 300

Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp
305                 310                 315                 320

Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly
325                 330                 335

Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn
340                 345                 350

Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp
355                 360                 365

Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro
370                 375                 380

Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu
385                 390                 395                 400

Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn
405                 410                 415

Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile
420                 425                 430

Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr
435                 440                 445

Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys
450                 455                 460

Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys
465                 470                 475                 480

Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu
485                 490                 495

Ser Leu Ser Pro Gly Lys
```

-continued

500

<210> SEQ ID NO 218
<211> LENGTH: 1515
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 218

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtgcagc tggtgcagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 120

tcctgtgcag cctctggatt caccttcagt agctatggca tgcactgggt ccgccaggct 180

ccaggcaagg ggctggagtg ggtggcagtt atatcatatg atggaagtat taaatactat 240

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 300

ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gcgaactggt 360

gaatatagtg gctacgatac gagtggttac agcaattggg gccaaggcac cctggtcacc 420

gtctcgagtg gtggaggcgg ttcaggcgga ggtggcagcg gcggtggcgg atcgcagtct 480

gtgctgactc agccaccctc agcgtctggg acccccgggc agagggtcac catctcttgt 540

tctggaagca gctccaacat cgggagtaac actgtaaact ggtaccagcg actcccagga 600

gcggcccccc aactcctcat ctacaataat gaccagcggc cctcagggat ccctgaccga 660

ttctctggct ccaagtctgg cacctcaggc tccctggtca tcagtgggct ccagtctgaa 720

gatgaggctg attactactg tgcgtcatgg gatgacagtc tgaatggtcg ggtgttcggc 780

ggagggacca agctgaccgt cctaggtgac gtacgcgagc ccaaatcttc tgacaaaact 840

cacacatgcc caccgtgccc agcacctgaa ctcctgggtg gaccgtcagt cttcctcttc 900

cccccaaaac ccaaggacac cctcatgatc tcccggaccc ctgaggtcac atgcgtggtg 960

gtggacgtga gccacgaaga ccctgaggtc aagttcaact ggtacgtgga cggcgtggag 1020

gtgcataatg ccaagacaaa gccgcgggag gagcagtaca acagcacgta ccgtgtggtc 1080

agcgtcctca ccgtcctgca ccaggactgg ctgaatggca aggagtacaa gtgcaaggtc 1140

tccaacaaag ccctcccagc ccccatcgag aaaaccatct ccaaagccaa agggcagccc 1200

cgagaaccac aggtgtacac cctgccccca tcccgggatg agctgaccaa gaaccaggtc 1260

agcctgacct gcctggtcaa aggcttctat ccaagcgaca tcgccgtgga gtgggagagc 1320

aatgggcagc cggagaacaa ctacaagacc acgcctcccg tgctggactc cgacggctcc 1380

ttcttcctct acagcaagct caccgtggac aagagcaggt ggcagcaggg gaacgtcttc 1440

tcatgctccg tgatgcatga ggctctgcac aaccactaca cgcagaagag cctctccctg 1500

tctccgggta aatga 1515

<210> SEQ ID NO 219
<211> LENGTH: 504
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

-continued

<400> SEQUENCE: 219

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Gly Gly Val Val
20 25 30

Gln Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Ile Lys Tyr Tyr
65 70 75 80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Arg Thr Gly Glu Tyr Ser Gly Tyr Asp Thr Ser
115 120 125

Gly Tyr Ser Asn Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser
145 150 155 160

Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln Arg Val
165 170 175

Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn Thr Val
180 185 190

Asn Trp Tyr Gln Arg Leu Pro Gly Ala Ala Pro Gln Leu Leu Ile Tyr
195 200 205

Asn Asn Asp Gln Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
210 215 220

Lys Ser Gly Thr Ser Gly Ser Leu Val Ile Ser Gly Leu Gln Ser Glu
225 230 235 240

Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Trp Asp Asp Ser Leu Asn Gly
245 250 255

Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg
260 265 270

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala
275 280 285

Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro
290 295 300

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val
305 310 315 320

Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val
325 330 335

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln
340 345 350

Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln
355 360 365

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala
370 375 380

Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro
385 390 395 400

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Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr
405                 410                 415

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser
420                 425                 430

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr
435                 440                 445

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr
450                 455                 460

Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe
465                 470                 475                 480

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys
485                 490                 495

Ser Leu Ser Leu Ser Pro Gly Lys
500
```

<210> SEQ ID NO 220
<211> LENGTH: 1488
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 220

```
atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

caggtgcagc tggtgcagtc tgggggaggc ttggtccagc cgggggggtc cctgagactc    120

tcctgtgcag cctctggatt cacgtttagt acctatgcca tgagttgggc ccgccaggct    180

ccagggaagg ggctggagtg ggtctcaagt attagtggtg atggtggaag aattctcgat    240

gcagactccg cgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat    300

ctgcaaatga acggcctgag agtcgaggac acggcccttt attactgtgc gagagcggac    360

ggtaactact ggggcagggg gacaatggtc accgtctctt caggtggagg cggttcaggc    420

ggaggtggca gcggcggtgg cggatcgcag tctgtgctga ctcagcctgc ctccgtgtct    480

gggtctcctg gacagtcgat caccatctcc tgcactggaa ccagcagtga cgttggtggt    540

tataactatg tctcctggta ccaacaacac ccaggcaaag cccccaaact catgatttat    600

gagggcagta agcggccctc aggggtttct aatcgcttct ctggctccaa gtctggcaac    660

acggcctccc tgacaatctc tgggctccag gctgaggacg aggctgatta ttactgcagc    720

tcatatacaa ccaggagcac tcgagttttc ggcggaggga ccaagctgac cgtcctaggt    780

gacgtacgcg agcccaaatc ttctgacaaa actcacacat gcccaccgtg cccagcacct    840

gaactcctgg gtggaccgtc agtcttcctc ttcccccaa aacccaagga caccctcatg    900

atctcccgga cccctgaggt cacatgcgtg gtggtggacg tgagccacga agaccctgag    960

gtcaagttca actggtacgt ggacggcgtg gaggtgcata atgccaagac aaagccgcgg   1020

gaggagcagt acaacagcac gtaccgtgtg gtcagcgtcc tcaccgtcct gcaccaggac   1080

tggctgaatg gcaaggagta caagtgcaag gtctccaaca aagccctccc agcccccatc   1140

gagaaaacca tctccaaagc caaagggcag ccccgagaac cacaggtgta caccctgccc   1200

ccatcccggg atgagctgac caagaaccag gtcagcctga cctgcctggt caaaggcttc   1260
```

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tatccaagcg acatcgccgt ggagtgggag agcaatgggc agccggagaa caactacaag 1320

accacgcctc ccgtgctgga ctccgacggc tccttcttcc tctacagcaa gctcaccgtg 1380

gacaagagca ggtggcagca ggggaacgtc ttctcatgct ccgtgatgca tgaggctctg 1440

cacaaccact acacgcagaa gagcctctcc ctgtctccgg gtaaatga 1488

<210> SEQ ID NO 221
<211> LENGTH: 495
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 221

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Gln Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val
20 25 30

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Thr Tyr Ala Met Ser Trp Ala Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ser Ser Ile Ser Gly Asp Gly Gly Arg Ile Leu Asp
65 70 75 80

Ala Asp Ser Ala Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Gly Leu Arg Val Glu Asp Thr Ala
100 105 110

Leu Tyr Tyr Cys Ala Arg Ala Asp Gly Asn Tyr Trp Gly Arg Gly Thr
115 120 125

Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
130 135 140

Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro Ala Ser Val Ser
145 150 155 160

Gly Ser Pro Gly Gln Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser
165 170 175

Asp Val Gly Gly Tyr Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly
180 185 190

Lys Ala Pro Lys Leu Met Ile Tyr Glu Gly Ser Lys Arg Pro Ser Gly
195 200 205

Val Ser Asn Arg Phe Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu
210 215 220

Thr Ile Ser Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser
225 230 235 240

Ser Tyr Thr Thr Arg Ser Thr Arg Val Phe Gly Gly Gly Thr Lys Leu
245 250 255

Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser Ser Asp Lys Thr His
260 265 270

Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val
275 280 285

Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr
290 295 300

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Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu
305 310 315 320

Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys
325 330 335

Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser
340 345 350

Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys
355 360 365

Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile
370 375 380

Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro
385 390 395 400

Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu
405 410 415

Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn
420 425 430

Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser
435 440 445

Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg
450 455 460

Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu
465 470 475 480

His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
485 490 495

<210> SEQ ID NO 222
<211> LENGTH: 1506
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 222

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

caggtgcagc tgcaggagtc gggggggaggc gtggtccagc ctgggggggtc cctgagactc 120

tcctgtgcag cgtctggatt caccttcagt ggctatggca tgcactgggt ccgccaggct 180

ccaggcaagg ggctggagtg ggtggcatct gtacggaacg atggaagtaa tacatactac 240

acagactccg tgaaggaccg attcaccatc tccagagaca acaccaagaa cacgctgtat 300

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc caagtcgaga 360

agagtgatgt atggcacctc ctattacttt gactactggg gcagaggcac cctggtcacc 420

gtctcctcag gtggaggcgg ttcaggcgga ggtggcagcg gcggtggcgg atcgtctgag 480

ctgactcagg accctgctgt gtctgtggcc ttgggacaga cagtcaggat cacatgccaa 540

ggagacagcc tcagaagcta ttatgcaagc tggtaccagc agaagccagg acaggcccct 600

gtacttgtca tctatggtaa aaacaaccgg ccctcaggga tcccagaccg attctctggc 660

tccagctcag gaaacacagc ttccttgacc atcactgggg ctcaggcgga agatgaggct 720

gactattact gtaactcccg ggacagcagt ggtaaccatg tggtattcgg cggagggacc 780

aagctgaccg tcctaggtga cgtacgcgag cccaaatctt ctgacaaaac tcacacatgc 840

-continued

ccaccgtgcc cagcacctga actcctgggt ggaccgtcag tcttcctctt ccccccaaaa 900

cccaaggaca ccctcatgat ctcccggacc cctgaggtca catgcgtggt ggtggacgtg 960

agccacgaag accctgaggt caagttcaac tggtacgtgg acggcgtgga ggtgcataat 1020

gccaagacaa agccgcggga ggagcagtac aacagcacgt accgtgtggt cagcgtcctc 1080

accgtcctgc accaggactg gctgaatggc aaggagtaca agtgcaaggt ctccaacaaa 1140

gccctcccag cccccatcga gaaaaccatc tccaaagcca aagggcagcc ccgagaacca 1200

caggtgtaca ccctgccccc atcccgggat gagctgacca agaaccaggt cagcctgacc 1260

tgcctggtca aaggcttcta tccaagcgac atcgccgtgg agtgggagag caatgggcag 1320

ccggagaaca actacaagac cacgcctccc gtgctggact ccgacggctc cttcttcctc 1380

tacagcaagc tcaccgtgga caagagcagg tggcagcagg ggaacgtctt ctcatgctcc 1440

gtgatgcatg aggctctgca caaccactac acgcagaaga gcctctccct gtctccgggt 1500

aaatga 1506

<210> SEQ ID NO 223
<211> LENGTH: 501
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 223

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Gln Val Gln Leu Gln Glu Ser Gly Gly Gly Val Val
20 25 30

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Gly Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ala Ser Val Arg Asn Asp Gly Ser Asn Thr Tyr Tyr
65 70 75 80

Thr Asp Ser Val Lys Asp Arg Phe Thr Ile Ser Arg Asp Asn Thr Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Lys Ser Arg Arg Val Met Tyr Gly Thr Ser Tyr
115 120 125

Tyr Phe Asp Tyr Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly
130 135 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Glu
145 150 155 160

Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val Arg
165 170 175

Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Lys Asn
195 200 205

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Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly
210                 215                 220

Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu Ala
225                 230                 235                 240

Asp Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His Val Val Phe
245                 250                 255

Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys
260                 265                 270

Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu
275                 280                 285

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
290                 295                 300

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
305                 310                 315                 320

Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val
325                 330                 335

Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser
340                 345                 350

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
355                 360                 365

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala
370                 375                 380

Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
385                 390                 395                 400

Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln
405                 410                 415

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
420                 425                 430

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
435                 440                 445

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu
450                 455                 460

Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser
465                 470                 475                 480

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
485                 490                 495

Leu Ser Pro Gly Lys
500


<210> SEQ ID NO 224
<211> LENGTH: 1503
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolynucleotide"

<400> SEQUENCE: 224

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

caggtgcagc tgcaggagtc gggcgcagga ctggtgaagc cttcggggac cctgtccctc    120

acctgcgctg tctctggtgg ctccatcagc agtggtaact ggtggagttg ggtccgccag    180

cccccaggga aggggctgga gtggattggg gaaatctctc atagtgggag caccaactac    240
```

-continued

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aacccgtccc tcaagagtcg agtcaccata tcagtagaca agtccaagaa ccagttctcc    300

ctgaacctga gttctgtgac cgccgcagac acggccgtgt attactgtgc gagagtaagg    360

ggtacggtgg gggatacacg gggacctgac tactggggcc agggaaccct ggtcaccgtc    420

tcgagtggtg gaggcggttc aggcggaggt ggcagcggcg gtggcggatc gtctgagctg    480

actcaggacc ctgctgtgtc tgtggccttg ggacagacag tcaggatcac atgccaagga    540

gacagcctca gaagctatta tgcaagctgg taccagcaga agccaggaca ggcccctgta    600

cttgtcatct atggtaaaaa caaccggccc tcagggatcc cagaccgatt ctctggctcc    660

agctcaggaa acacagcttc cttgaccatc actggggctc aggcggaaga tgaggctgac    720

tattactgta actcccggga cagcagtggt aaccatgtgg tattcggcgg agggaccaag    780

ctgaccgtcc taggtgacgt acgcgagccc aaatcttctg acaaaactca cacatgccca    840

ccgtgcccag cacctgaact cctgggtgga ccgtcagtct tcctcttccc cccaaaaccc    900

aaggacaccc tcatgatctc ccggacccct gaggtcacat gcgtggtggt ggacgtgagc    960

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc   1020

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc   1080

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc   1140

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag   1200

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc   1260

ctggtcaaag gcttctatcc aagcgacatc gccgtggagt gggagagcaa tgggcagccg   1320

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac   1380

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg   1440

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa   1500

tga                                                                 1503
```

<210> SEQ ID NO 225
<211> LENGTH: 500
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 225

```
Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1               5                  10                  15

Asp Thr Thr Gly Gln Val Gln Leu Gln Glu Ser Gly Ala Gly Leu Val
20                  25                  30

Lys Pro Ser Gly Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser
35                  40                  45

Ile Ser Ser Gly Asn Trp Trp Ser Trp Val Arg Gln Pro Pro Gly Lys
50                  55                  60

Gly Leu Glu Trp Ile Gly Glu Ile Ser His Ser Gly Ser Thr Asn Tyr
65                  70                  75                  80

Asn Pro Ser Leu Lys Ser Arg Val Thr Ile Ser Val Asp Lys Ser Lys
85                  90                  95

Asn Gln Phe Ser Leu Asn Leu Ser Ser Val Thr Ala Ala Asp Thr Ala
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100                 105                 110

Val Tyr Tyr Cys Ala Arg Val Arg Gly Thr Val Gly Asp Thr Arg Gly
115                 120                 125

Pro Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly
130                 135                 140

Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ser Glu Leu
145                 150                 155                 160

Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln Thr Val Arg Ile
165                 170                 175

Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala Ser Trp Tyr Gln
180                 185                 190

Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr Gly Lys Asn Asn
195                 200                 205

Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser Ser Ser Gly Asn
210                 215                 220

Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu Asp Glu Ala Asp
225                 230                 235                 240

Tyr Tyr Cys Asn Ser Arg Asp Ser Ser Gly Asn His Val Val Phe Gly
245                 250                 255

Gly Gly Thr Lys Leu Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser
260                 265                 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
275                 280                 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385                 390                 395                 400

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
405                 410                 415

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
485                 490                 495

Ser Pro Gly Lys
500
```

-continued

<210> SEQ ID NO 226
<211> LENGTH: 1503
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 226

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtgcagc tggtgcagtc tgggggaggc ctggtcaagc ctgggggggtc cctgagactc 120

tcctgtgcag cgtctggatt caccttcagt agctatggga tgcactgggt ccgccaggct 180

ccaggcaagg ggctggagtg ggtggcaggt atttttttatg atggaggtaa taaatactat 240

gcagactccg tgaagggccg attcaccatc tccagagaca attccaagaa cacgctgtat 300

ctgcaaatga acagcctgag agctgaggac acggctgtgt attactgtgc gagagatagg 360

ggctactact acatggacgt ctggggcaaa gggaccacgg tcaccgtctc ctcaggtgga 420

ggcggttcag gcggaggtgg ctctggcggt ggcggatcgc agtctgtgtt gacgcagccg 480

ccctcagtgt ctggggcccc aggacagagg gtcaccatct cctgcactgg gagaagctcc 540

aacatcgggg cgggtcatga tgtacactgg taccagcaac ttccaggaac agcccccaaa 600

ctcctcatct atggtgacag caatcggccc tcaggggtcc ctgaccgatt ctctggctcc 660

aggtctggca cctcagcctc cctggccatc actgggctcc aggctgaaga tgaggctgat 720

tattactgcc agtcctatga cagcagcctg aggggttcgg tattcggcgg agggaccaag 780

gtcaccgtcc taggtgacgt acgcgagccc aaatcttctg acaaaactca cacatgccca 840

ccgtgcccag cacctgaact cctgggtgga ccgtcagtct tcctcttccc cccaaaaccc 900

aaggacaccc tcatgatctc ccggaccccct gaggtcacat gcgtggtggt ggacgtgagc 960

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc 1020

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc 1080

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc 1140

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag 1200

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc 1260

ctggtcaaag gcttctatcc aagcgacatc gccgtggagt gggagagcaa tgggcagccg 1320

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac 1380

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg 1440

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa 1500

tga 1503

<210> SEQ ID NO 227
<211> LENGTH: 500
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 227

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```
Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1               5                  10                  15

Asp Thr Thr Gly Glu Val Gln Leu Val Gln Ser Gly Gly Gly Leu Val
20                  25                  30

Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35                  40                  45

Phe Ser Ser Tyr Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly
50                  55                  60

Leu Glu Trp Val Ala Gly Ile Phe Tyr Asp Gly Gly Asn Lys Tyr Tyr
65                  70                  75                  80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100                 105                 110

Val Tyr Tyr Cys Ala Arg Asp Arg Gly Tyr Tyr Tyr Met Asp Val Trp
115                 120                 125

Gly Lys Gly Thr Thr Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly
130                 135                 140

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gln Ser Val Leu Thr Gln Pro
145                 150                 155                 160

Pro Ser Val Ser Gly Ala Pro Gly Gln Arg Val Thr Ile Ser Cys Thr
165                 170                 175

Gly Arg Ser Ser Asn Ile Gly Ala Gly His Asp Val His Trp Tyr Gln
180                 185                 190

Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu Ile Tyr Gly Asp Ser Asn
195                 200                 205

Arg Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Arg Ser Gly Thr
210                 215                 220

Ser Ala Ser Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp
225                 230                 235                 240

Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser Leu Arg Gly Ser Val Phe Gly
245                 250                 255

Gly Gly Thr Lys Val Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser
260                 265                 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
275                 280                 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385                 390                 395                 400
```

-continued

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
405 410 415

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
420 425 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
435 440 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
450 455 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465 470 475 480

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
485 490 495

Ser Pro Gly Lys
500

<210> SEQ ID NO 228
<211> LENGTH: 1500
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 228

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc 120

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct 180

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac 240

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat 300

ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagaggcggg 360

agtgggagtg actactgggg ccaggggaca atggtcaccg tctcgagtgg aggcggcggt 420

tcaggcggag gtggctctgg cggtggcgga agtgcactta attttatgct gactcagccc 480

cactctgtgt cggggtctcc ggggaagacg gtaaccatct cctgcacccg cagcagtggc 540

tacattgaca gcaagtatgt gcagtggtac cagcagcgcc cgggcagtgc ccccaccact 600

gtgatctatg aggataaccg aagaccctct ggggtccctg atcggttctc tggctccatc 660

gacagctcct ccaactctgc ctccctcacc atctctggac tggagactga ggacgaggct 720

gactattact gtcagtctta tgatgacacc aatgtggtgt tcggcggagg gaccaaggtc 780

accgtcctag gtgacgtacg cgagcccaaa tcttctgaca aaactcacac atgcccaccg 840

tgcccagcac ctgaactcct gggtggaccg tcagtcttcc tcttcccccc aaaacccaag 900

gacaccctca tgatctcccg gacccctgag gtcacatgcg tggtggtgga cgtgagccac 960

gaagaccctg aggtcaagtt caactggtac gtggacggcg tggaggtgca taatgccaag 1020

acaaagccgc gggaggagca gtacaacagc acgtaccgtg tggtcagcgt cctcaccgtc 1080

ctgcaccagg actggctgaa tggcaaggag tacaagtgca aggtctccaa caaagccctc 1140

ccagccccca tcgagaaaac catctccaaa gccaaagggc agccccgaga accacaggtg 1200

tacaccctgc ccccatcccg ggatgagctg accaagaacc aggtcagcct gacctgcctg 1260

gtcaaaggct tctatccaag cgacatcgcc gtggagtggg agagcaatgg gcagccggag 1320

-continued

aacaactaca agaccacgcc tcccgtgctg gactccgacg gctccttctt cctctacagc 1380

aagctcaccg tggacaagag caggtggcag caggggaacg tcttctcatg ctccgtgatg 1440

catgaggctc tgcacaacca ctacacgcag aagagcctct ccctgtctcc gggtaaatga 1500

<210> SEQ ID NO 229
<211> LENGTH: 499
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 229

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val
20 25 30

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Arg Gly Gly Ser Gly Ser Asp Tyr Trp Gly Gln
115 120 125

Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Ala Leu Asn Phe Met Leu Thr Gln Pro
145 150 155 160

His Ser Val Ser Gly Ser Pro Gly Lys Thr Val Thr Ile Ser Cys Thr
165 170 175

Arg Ser Ser Gly Tyr Ile Asp Ser Lys Tyr Val Gln Trp Tyr Gln Gln
180 185 190

Arg Pro Gly Ser Ala Pro Thr Thr Val Ile Tyr Glu Asp Asn Arg Arg
195 200 205

Pro Ser Gly Val Pro Asp Arg Phe Ser Gly Ser Ile Asp Ser Ser Ser
210 215 220

Asn Ser Ala Ser Leu Thr Ile Ser Gly Leu Glu Thr Glu Asp Glu Ala
225 230 235 240

Asp Tyr Tyr Cys Gln Ser Tyr Asp Asp Thr Asn Val Val Phe Gly Gly
245 250 255

Gly Thr Lys Val Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser Ser
260 265 270

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
275 280 285

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
290 295 300

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```
Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
305                 310                 315                 320

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
325                 330                 335

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
340                 345                 350

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
355                 360                 365

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
370                 375                 380

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
385                 390                 395                 400

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
405                 410                 415

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
420                 425                 430

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
435                 440                 445

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
450                 455                 460

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
465                 470                 475                 480

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
485                 490                 495

Pro Gly Lys
```

<210> SEQ ID NO 230
<211> LENGTH: 1500
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 230

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atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

ggggtgcagc tggtggagtc tgggggaggc ctggtcaagc ctgggggggtc cctgagactc    120

tcctgtgcag cctctggatt caccttcagt agctataaca tgaactgggt ccgccaggct    180

ccagggaagg gactggagtg ggtctcagct attagtggta gtggtggtag cacatactac    240

gcagactccg tgacgggccg gttcaccatc tccagagaca attccaagaa cacgctgtat    300

ctgcaaatga acagcctgag agccgaggac acggccgtat attactgtgc gaaagatacc    360

agtggctggt acggggacgg tatggacgtc tggggccggg gaaccctggt caccgtctcg    420

agtggtggag gcggttcagg cggaggtggc agcggcggtg gcggatcgga catccagatg    480

acccagtctc cttccaccct gtctgcatct attggagaca gagtcaccat cacctgccgg    540

gccagtgagg gtatttatca ctggttggcc tggtatcagc agaagccagg gaaagccct     600

aaactcctga tctataaggc ctctagttta gccagtgggg ccccatcaag gttcagcggc    660

agtggatcag ggacagattt cactctcacc atcagcagcc tgcagcctga tgattttgca    720

acttattact gccaacaata tagtaattat ccgctcactt tcggcggagg gaccaagctg    780
```

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gagatcaaac gtgacgtacg cgagcccaaa tcttctgaca aaactcacac atgcccaccg 840

tgcccagcac ctgaactcct gggtggaccg tcagtcttcc tcttcccccc aaaacccaag 900

gacaccctca tgatctcccg gacccctgag gtcacatgcg tggtggtgga cgtgagccac 960

gaagaccctg aggtcaagtt caactggtac gtggacggcg tggaggtgca taatgccaag 1020

acaaagccgc gggaggagca gtacaacagc acgtaccgtg tggtcagcgt cctcaccgtc 1080

ctgcaccagg actggctgaa tggcaaggag tacaagtgca aggtctccaa caaagccctc 1140

ccagccccca tcgagaaaac catctccaaa gccaaagggc agccccgaga accacaggtg 1200

tacaccctgc ccccatcccg ggatgagctg accaagaacc aggtcagcct gacctgcctg 1260

gtcaaaggct tctatccaag cgacatcgcc gtggagtggg agagcaatgg gcagccggag 1320

aacaactaca agaccacgcc tcccgtgctg gactccgacg gctccttctt cctctacagc 1380

aagctcaccg tggacaagag caggtggcag caggggaacg tcttctcatg ctccgtgatg 1440

catgaggctc tgcacaacca ctacacgcag aagagcctct ccctgtctcc gggtaaatga 1500

<210> SEQ ID NO 231
<211> LENGTH: 499
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 231

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly Gly Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val
20 25 30

Lys Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35 40 45

Phe Ser Ser Tyr Asn Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly
50 55 60

Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr
65 70 75 80

Ala Asp Ser Val Thr Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85 90 95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100 105 110

Val Tyr Tyr Cys Ala Lys Asp Thr Ser Gly Trp Tyr Gly Asp Gly Met
115 120 125

Asp Val Trp Gly Arg Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly
130 135 140

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Asp Ile Gln Met
145 150 155 160

Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Ile Gly Asp Arg Val Thr
165 170 175

Ile Thr Cys Arg Ala Ser Glu Gly Ile Tyr His Trp Leu Ala Trp Tyr
180 185 190

Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr Lys Ala Ser
195 200 205

Ser Leu Ala Ser Gly Ala Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly

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210                 215                 220

Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Asp Asp Phe Ala
225                 230                 235                 240

Thr Tyr Tyr Cys Gln Gln Tyr Ser Asn Tyr Pro Leu Thr Phe Gly Gly
245                 250                 255

Gly Thr Lys Leu Glu Ile Lys Arg Asp Val Arg Glu Pro Lys Ser Ser
260                 265                 270

Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly
275                 280                 285

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met
290                 295                 300

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His
305                 310                 315                 320

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val
325                 330                 335

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr
340                 345                 350

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly
355                 360                 365

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile
370                 375                 380

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val
385                 390                 395                 400

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser
405                 410                 415

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu
420                 425                 430

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro
435                 440                 445

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val
450                 455                 460

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met
465                 470                 475                 480

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser
485                 490                 495

Pro Gly Lys
```

<210> SEQ ID NO 232
<211> LENGTH: 1503
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 232

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atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt     60

gaggtgcagc tgttggagtc tgggggaggc ttggtacagc ctgggggggtc cctgagactc    120

tcctgtgcag cctctggatt cacctttagc agctatgcca tgagctgggt ccgccaggct    180

ccagggaagg ggctggagtg ggtctcagct attagtggta gtggtggtag cacatactac    240

gcagactccg tgaagggccg gttcaccatc tccagagaca attccaagaa cacgctgtat    300
```

-continued

```
ctgcaaatga acagcctgag agccgaggac acggccgtgt attactgtgc gagagtcagc    360

gggagccact ttccattctt tgactcctgg ggccagggga caatggtcac cgtctcgagt    420

ggaggcggcg gttcaggcgg aggtggctct ggcggtggcg gaagtgcaca gtctgtgctg    480

actcagccac cctcggtgtc agtggcccca ggacagacgg ccagaattac ctgtggggga    540

gacaagattg gacataaaag tgtgcattgg tatcagcaga agccaggcca ggcccctgtg    600

ttgctcgtct atgatgatag gaagcggccc tcagggatcc ctgagcgatt ctctggctcc    660

aactctggga acacggccac cctgaccatc agcagggtcg aggccgggga tgaggctgcc    720

tatcactgtc aggtgtggga tagaagtagt gacccttatg tcttcggaac tgggaccaag    780

gtcaccgtcc taggtgacgt acgcgagccc aaatcttctg acaaaactca cacatgccca    840

ccgtgcccag cacctgaact cctgggtgga ccgtcagtct tcctcttccc cccaaaaccc    900

aaggacaccc tcatgatctc ccggaccccc gaggtcacat gcgtggtggt ggacgtgagc    960

cacgaagacc ctgaggtcaa gttcaactgg tacgtggacg gcgtggaggt gcataatgcc   1020

aagacaaagc cgcgggagga gcagtacaac agcacgtacc gtgtggtcag cgtcctcacc   1080

gtcctgcacc aggactggct gaatggcaag gagtacaagt gcaaggtctc caacaaagcc   1140

ctcccagccc ccatcgagaa aaccatctcc aaagccaaag ggcagccccg agaaccacag   1200

gtgtacaccc tgcccccatc ccgggatgag ctgaccaaga accaggtcag cctgacctgc   1260

ctggtcaaag gcttctatcc aagcgacatc gccgtggagt gggagagcaa tgggcagccg   1320

gagaacaact acaagaccac gcctcccgtg ctggactccg acggctcctt cttcctctac   1380

agcaagctca ccgtggacaa gagcaggtgg cagcagggga acgtcttctc atgctccgtg   1440

atgcatgagg ctctgcacaa ccactacacg cagaagagcc tctccctgtc tccgggtaaa   1500

tga                                                                1503
```

<210> SEQ ID NO 233
<211> LENGTH: 500
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 233

```
Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1               5                   10                  15

Asp Thr Thr Gly Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val
20                  25                  30

Gln Pro Gly Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr
35                  40                  45

Phe Ser Ser Tyr Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly
50                  55                  60

Leu Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr
65                  70                  75                  80

Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys
85                  90                  95

Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala
100                 105                 110
```

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```
Val Tyr Tyr Cys Ala Arg Val Ser Gly Ser His Phe Pro Phe Phe Asp
115                 120                 125

Ser Trp Gly Gln Gly Thr Met Val Thr Val Ser Ser Gly Gly Gly Gly
130                 135                 140

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Ala Gln Ser Val Leu
145                 150                 155                 160

Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln Thr Ala Arg Ile
165                 170                 175

Thr Cys Gly Gly Asp Lys Ile Gly His Lys Ser Val His Trp Tyr Gln
180                 185                 190

Gln Lys Pro Gly Gln Ala Pro Val Leu Leu Val Tyr Asp Asp Arg Lys
195                 200                 205

Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser Asn Ser Gly Asn
210                 215                 220

Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly Asp Glu Ala Ala
225                 230                 235                 240

Tyr His Cys Gln Val Trp Asp Arg Ser Ser Asp Pro Tyr Val Phe Gly
245                 250                 255

Thr Gly Thr Lys Val Thr Val Leu Gly Asp Val Arg Glu Pro Lys Ser
260                 265                 270

Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
275                 280                 285

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
290                 295                 300

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
305                 310                 315                 320

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
325                 330                 335

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr
340                 345                 350

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn
355                 360                 365

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro
370                 375                 380

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln
385                 390                 395                 400

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val
405                 410                 415

Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val
420                 425                 430

Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro
435                 440                 445

Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr
450                 455                 460

Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val
465                 470                 475                 480

Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu
485                 490                 495

Ser Pro Gly Lys
500
```

-continued

<210> SEQ ID NO 234
<211> LENGTH: 60
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticoligonucleotide"

<400> SEQUENCE: 234

atggaagcac cagcgcagct tctcttcctc ctgctactct ggctcccaga taccaccggt 60

<210> SEQ ID NO 235
<211> LENGTH: 20
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpeptide"

<400> SEQUENCE: 235

Met Glu Ala Pro Ala Gln Leu Leu Phe Leu Leu Leu Leu Trp Leu Pro
1 5 10 15

Asp Thr Thr Gly
20

<210> SEQ ID NO 236
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticoligonucleotide"

<400> SEQUENCE: 236

ggaggcggcg gttcaggcgg aggtggctct ggcggtggcg gaagt 45

<210> SEQ ID NO 237
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpeptide"

<400> SEQUENCE: 237

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
1 5 10 15

<210> SEQ ID NO 238
<211> LENGTH: 45
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticoligonucleotide"

<400> SEQUENCE: 238

gagcccaaat cttctgacaa aactcacaca tgcccaccgt gccca 45

<210> SEQ ID NO 239

-continued

<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpeptide"

<400> SEQUENCE: 239

Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro Cys Pro
1 5 10 15

<210> SEQ ID NO 240
<211> LENGTH: 708
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolynucleotide"

<400> SEQUENCE: 240

gacgtacgcg agcccaaatc ttctgacaaa actcacacat gcccaccgtg cccagcacct 60

gaactcctgg gtggaccgtc agtcttcctc ttcccccaa aacccaagga caccctcatg 120

atctcccgga cccctgaggt cacatgcgtg gtggtggacg tgagccacga agaccctgag 180

gtcaagttca actggtacgt ggacggcgtg gaggtgcata atgccaagac aaagccgcgg 240

gaggagcagt acaacagcac gtaccgtgtg gtcagcgtcc tcaccgtcct gcaccaggac 300

tggctgaatg gcaaggagta caagtgcaag gtctccaaca aagccctccc agccccatc 360

gagaaaacca tctccaaagc caaagggcag ccccgagaac cacaggtgta caccctgccc 420

ccatcccggg atgagctgac caagaaccag gtcagcctga cctgcctggt caaaggcttc 480

tatccaagcg acatcgccgt ggagtgggag agcaatgggc agccggagaa caactacaag 540

accacgcctc ccgtgctgga ctccgacggc tccttcttcc tctacagcaa gctcaccgtg 600

gacaagagca ggtggcagca ggggaacgtc ttctcatgct ccgtgatgca tgaggctctg 660

cacaaccact acacgcagaa gagcctctcc ctgtctccgg gtaaatga 708

<210> SEQ ID NO 241
<211> LENGTH: 235
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 241

Asp Val Arg Glu Pro Lys Ser Ser Asp Lys Thr His Thr Cys Pro Pro
1 5 10 15

Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn
50 55 60

Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg
65 70 75 80

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```
Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val
85                  90                  95

Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser
100                 105                 110

Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys
115                 120                 125

Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp
130                 135                 140

Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe
145                 150                 155                 160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu
165                 170                 175

Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe
180                 185                 190

Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly
195                 200                 205

Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr
210                 215                 220

Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys
225                 230                 235


<210> SEQ ID NO 242
<211> LENGTH: 656
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 242

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1               5                   10                  15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20                  25                  30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35                  40                  45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50                  55                  60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85                  90                  95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100                 105                 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115                 120                 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130                 135                 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165                 170                 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
```

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```
180                 185                 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195                 200                 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210                 215                 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245                 250                 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260                 265                 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275                 280                 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290                 295                 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325                 330                 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
340                 345                 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
355                 360                 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
370                 375                 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
405                 410                 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
420                 425                 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
435                 440                 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
450                 455                 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
485                 490                 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
500                 505                 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
515                 520                 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
530                 535                 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
565                 570                 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
580                 585                 590
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```
Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
595                 600                 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
610                 615                 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625                 630                 635                 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
645                 650                 655


<210> SEQ ID NO 243
<211> LENGTH: 647
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 243

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1               5                   10                  15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20                  25                  30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35                  40                  45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50                  55                  60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85                  90                  95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100                 105                 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115                 120                 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130                 135                 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165                 170                 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180                 185                 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195                 200                 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210                 215                 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245                 250                 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260                 265                 270
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```
Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275                 280                 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290                 295                 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325                 330                 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
340                 345                 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
355                 360                 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
370                 375                 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
405                 410                 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
420                 425                 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
435                 440                 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
450                 455                 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
485                 490                 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
500                 505                 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
515                 520                 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
530                 535                 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
565                 570                 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
580                 585                 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
595                 600                 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
610                 615                 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625                 630                 635                 640

Gly Cys Pro Ala Glu Gln Arg
645


<210> SEQ ID NO 244
<211> LENGTH: 599
<212> TYPE: PRT
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-continued

<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 244

```
Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1               5                  10                  15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20                  25                  30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35                  40                  45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50                  55                  60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85                  90                  95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100                 105                 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115                 120                 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130                 135                 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165                 170                 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180                 185                 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195                 200                 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210                 215                 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245                 250                 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260                 265                 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275                 280                 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290                 295                 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325                 330                 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
340                 345                 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
355                 360                 365
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```
Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
370                 375                 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
405                 410                 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
420                 425                 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
435                 440                 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
450                 455                 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
485                 490                 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
500                 505                 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
515                 520                 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
530                 535                 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
565                 570                 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
580                 585                 590

Pro Pro Phe Cys Val Ala Arg
595


<210> SEQ ID NO 245
<211> LENGTH: 338
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 245

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1               5                   10                  15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20                  25                  30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35                  40                  45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50                  55                  60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85                  90                  95
```

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```
Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100                 105                 110

Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115                 120                 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130                 135                 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165                 170                 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180                 185                 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195                 200                 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210                 215                 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245                 250                 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260                 265                 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275                 280                 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290                 295                 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325                 330                 335

Pro Cys


<210> SEQ ID NO 246
<211> LENGTH: 1255
<212> TYPE: PRT
<213> ORGANISM: Homo sapiens

<400> SEQUENCE: 246

Met Glu Leu Ala Ala Leu Cys Arg Trp Gly Leu Leu Leu Ala Leu Leu
1               5                   10                  15

Pro Pro Gly Ala Ala Ser Thr Gln Val Cys Thr Gly Thr Asp Met Lys
20                  25                  30

Leu Arg Leu Pro Ala Ser Pro Glu Thr His Leu Asp Met Leu Arg His
35                  40                  45

Leu Tyr Gln Gly Cys Gln Val Val Gln Gly Asn Leu Glu Leu Thr Tyr
50                  55                  60

Leu Pro Thr Asn Ala Ser Leu Ser Phe Leu Gln Asp Ile Gln Glu Val
65                  70                  75                  80

Gln Gly Tyr Val Leu Ile Ala His Asn Gln Val Arg Gln Val Pro Leu
85                  90                  95

Gln Arg Leu Arg Ile Val Arg Gly Thr Gln Leu Phe Glu Asp Asn Tyr
100                 105                 110
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```
Ala Leu Ala Val Leu Asp Asn Gly Asp Pro Leu Asn Asn Thr Thr Pro
115                 120                 125

Val Thr Gly Ala Ser Pro Gly Gly Leu Arg Glu Leu Gln Leu Arg Ser
130                 135                 140

Leu Thr Glu Ile Leu Lys Gly Gly Val Leu Ile Gln Arg Asn Pro Gln
145                 150                 155                 160

Leu Cys Tyr Gln Asp Thr Ile Leu Trp Lys Asp Ile Phe His Lys Asn
165                 170                 175

Asn Gln Leu Ala Leu Thr Leu Ile Asp Thr Asn Arg Ser Arg Ala Cys
180                 185                 190

His Pro Cys Ser Pro Met Cys Lys Gly Ser Arg Cys Trp Gly Glu Ser
195                 200                 205

Ser Glu Asp Cys Gln Ser Leu Thr Arg Thr Val Cys Ala Gly Gly Cys
210                 215                 220

Ala Arg Cys Lys Gly Pro Leu Pro Thr Asp Cys Cys His Glu Gln Cys
225                 230                 235                 240

Ala Ala Gly Cys Thr Gly Pro Lys His Ser Asp Cys Leu Ala Cys Leu
245                 250                 255

His Phe Asn His Ser Gly Ile Cys Glu Leu His Cys Pro Ala Leu Val
260                 265                 270

Thr Tyr Asn Thr Asp Thr Phe Glu Ser Met Pro Asn Pro Glu Gly Arg
275                 280                 285

Tyr Thr Phe Gly Ala Ser Cys Val Thr Ala Cys Pro Tyr Asn Tyr Leu
290                 295                 300

Ser Thr Asp Val Gly Ser Cys Thr Leu Val Cys Pro Leu His Asn Gln
305                 310                 315                 320

Glu Val Thr Ala Glu Asp Gly Thr Gln Arg Cys Glu Lys Cys Ser Lys
325                 330                 335

Pro Cys Ala Arg Val Cys Tyr Gly Leu Gly Met Glu His Leu Arg Glu
340                 345                 350

Val Arg Ala Val Thr Ser Ala Asn Ile Gln Glu Phe Ala Gly Cys Lys
355                 360                 365

Lys Ile Phe Gly Ser Leu Ala Phe Leu Pro Glu Ser Phe Asp Gly Asp
370                 375                 380

Pro Ala Ser Asn Thr Ala Pro Leu Gln Pro Glu Gln Leu Gln Val Phe
385                 390                 395                 400

Glu Thr Leu Glu Glu Ile Thr Gly Tyr Leu Tyr Ile Ser Ala Trp Pro
405                 410                 415

Asp Ser Leu Pro Asp Leu Ser Val Phe Gln Asn Leu Gln Val Ile Arg
420                 425                 430

Gly Arg Ile Leu His Asn Gly Ala Tyr Ser Leu Thr Leu Gln Gly Leu
435                 440                 445

Gly Ile Ser Trp Leu Gly Leu Arg Ser Leu Arg Glu Leu Gly Ser Gly
450                 455                 460

Leu Ala Leu Ile His His Asn Thr His Leu Cys Phe Val His Thr Val
465                 470                 475                 480

Pro Trp Asp Gln Leu Phe Arg Asn Pro His Gln Ala Leu Leu His Thr
485                 490                 495

Ala Asn Arg Pro Glu Asp Glu Cys Val Gly Glu Gly Leu Ala Cys His
500                 505                 510

Gln Leu Cys Ala Arg Gly His Cys Trp Gly Pro Gly Pro Thr Gln Cys
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515                 520                 525

Val Asn Cys Ser Gln Phe Leu Arg Gly Gln Glu Cys Val Glu Glu Cys
530                 535                 540

Arg Val Leu Gln Gly Leu Pro Arg Glu Tyr Val Asn Ala Arg His Cys
545                 550                 555                 560

Leu Pro Cys His Pro Glu Cys Gln Pro Gln Asn Gly Ser Val Thr Cys
565                 570                 575

Phe Gly Pro Glu Ala Asp Gln Cys Val Ala Cys Ala His Tyr Lys Asp
580                 585                 590

Pro Pro Phe Cys Val Ala Arg Cys Pro Ser Gly Val Lys Pro Asp Leu
595                 600                 605

Ser Tyr Met Pro Ile Trp Lys Phe Pro Asp Glu Glu Gly Ala Cys Gln
610                 615                 620

Pro Cys Pro Ile Asn Cys Thr His Ser Cys Val Asp Leu Asp Asp Lys
625                 630                 635                 640

Gly Cys Pro Ala Glu Gln Arg Ala Ser Pro Leu Thr Ser Ile Ile Ser
645                 650                 655

Ala Val Val Gly Ile Leu Leu Val Val Val Leu Gly Val Val Phe Gly
660                 665                 670

Ile Leu Ile Lys Arg Arg Gln Gln Lys Ile Arg Lys Tyr Thr Met Arg
675                 680                 685

Arg Leu Leu Gln Glu Thr Glu Leu Val Glu Pro Leu Thr Pro Ser Gly
690                 695                 700

Ala Met Pro Asn Gln Ala Gln Met Arg Ile Leu Lys Glu Thr Glu Leu
705                 710                 715                 720

Arg Lys Val Lys Val Leu Gly Ser Gly Ala Phe Gly Thr Val Tyr Lys
725                 730                 735

Gly Ile Trp Ile Pro Asp Gly Glu Asn Val Lys Ile Pro Val Ala Ile
740                 745                 750

Lys Val Leu Arg Glu Asn Thr Ser Pro Lys Ala Asn Lys Glu Ile Leu
755                 760                 765

Asp Glu Ala Tyr Val Met Ala Gly Val Gly Ser Pro Tyr Val Ser Arg
770                 775                 780

Leu Leu Gly Ile Cys Leu Thr Ser Thr Val Gln Leu Val Thr Gln Leu
785                 790                 795                 800

Met Pro Tyr Gly Cys Leu Leu Asp His Val Arg Glu Asn Arg Gly Arg
805                 810                 815

Leu Gly Ser Gln Asp Leu Leu Asn Trp Cys Met Gln Ile Ala Lys Gly
820                 825                 830

Met Ser Tyr Leu Glu Asp Val Arg Leu Val His Arg Asp Leu Ala Ala
835                 840                 845

Arg Asn Val Leu Val Lys Ser Pro Asn His Val Lys Ile Thr Asp Phe
850                 855                 860

Gly Leu Ala Arg Leu Leu Asp Ile Asp Glu Thr Glu Tyr His Ala Asp
865                 870                 875                 880

Gly Gly Lys Val Pro Ile Lys Trp Met Ala Leu Glu Ser Ile Leu Arg
885                 890                 895

Arg Arg Phe Thr His Gln Ser Asp Val Trp Ser Tyr Gly Val Thr Val
900                 905                 910

Trp Glu Leu Met Thr Phe Gly Ala Lys Pro Tyr Asp Gly Ile Pro Ala
915                 920                 925
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Arg Glu Ile Pro Asp Leu Leu Glu Lys Gly Glu Arg Leu Pro Gln Pro
930                 935                 940

Pro Ile Cys Thr Ile Asp Val Tyr Met Ile Met Val Lys Cys Trp Met
945                 950                 955                 960

Ile Asp Ser Glu Cys Arg Pro Arg Phe Arg Glu Leu Val Ser Glu Phe
965                 970                 975

Ser Arg Met Ala Arg Asp Pro Gln Arg Phe Val Val Ile Gln Asn Glu
980                 985                 990

Asp Leu Gly Pro Ala Ser Pro Leu  Asp Ser Thr Phe Tyr  Arg Ser Leu
995                 1000                1005

Leu Glu  Asp Asp Asp Met Gly  Asp Leu Val Asp Ala  Glu Glu Tyr
1010                1015                1020

Leu Val  Pro Gln Gln Gly Phe  Phe Cys Pro Asp Pro  Ala Pro Gly
1025                1030                1035

Ala Gly  Gly Met Val His His  Arg His Arg Ser Ser  Ser Thr Arg
1040                1045                1050

Ser Gly  Gly Gly Asp Leu Thr  Leu Gly Leu Glu Pro  Ser Glu Glu
1055                1060                1065

Glu Ala  Pro Arg Ser Pro Leu  Ala Pro Ser Glu Gly  Ala Gly Ser
1070                1075                1080

Asp Val  Phe Asp Gly Asp Leu  Gly Met Gly Ala Ala  Lys Gly Leu
1085                1090                1095

Gln Ser  Leu Pro Thr His Asp  Pro Ser Pro Leu Gln  Arg Tyr Ser
1100                1105                1110

Glu Asp  Pro Thr Val Pro Leu  Pro Ser Glu Thr Asp  Gly Tyr Val
1115                1120                1125

Ala Pro  Leu Thr Cys Ser Pro  Gln Pro Glu Tyr Val  Asn Gln Pro
1130                1135                1140

Asp Val  Arg Pro Gln Pro Pro  Ser Pro Arg Glu Gly  Pro Leu Pro
1145                1150                1155

Ala Ala  Arg Pro Ala Gly Ala  Thr Leu Glu Arg Pro  Lys Thr Leu
1160                1165                1170

Ser Pro  Gly Lys Asn Gly Val  Val Lys Asp Val Phe  Ala Phe Gly
1175                1180                1185

Gly Ala  Val Glu Asn Pro Glu  Tyr Leu Thr Pro Gln  Gly Gly Ala
1190                1195                1200

Ala Pro  Gln Pro His Pro Pro  Pro Ala Phe Ser Pro  Ala Phe Asp
1205                1210                1215

Asn Leu  Tyr Tyr Trp Asp Gln  Asp Pro Pro Glu Arg  Gly Ala Pro
1220                1225                1230

Pro Ser  Thr Phe Lys Gly Thr  Pro Thr Ala Glu Asn  Pro Glu Tyr
1235                1240                1245

Leu Gly  Leu Asp Val Pro Val
1250                1255


<210> SEQ ID NO 247
<211> LENGTH: 20
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticprimer"
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<400> SEQUENCE: 247

ggaaacagct atgaccatga 20

<210> SEQ ID NO 248
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticprimer"

<400> SEQUENCE: 248

ctcttctgag atgagttttt g 21

<210> SEQ ID NO 249
<211> LENGTH: 18
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticprimer"

<400> SEQUENCE: 249

ggagattttc aacgtgaa 18

<210> SEQ ID NO 250
<211> LENGTH: 21
<212> TYPE: DNA
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticprimer"

<400> SEQUENCE: 250

ctcttctgag atgagttttt g 21

<210> SEQ ID NO 251
<211> LENGTH: 5
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpeptide"

<400> SEQUENCE: 251

Gly Gly Gly Gly Ser
1 5

<210> SEQ ID NO 252
<211> LENGTH: 97
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 252

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

-continued

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Gly Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Ser Ala Tyr Asn Gly Asn Thr Asn Tyr Ala Gln Lys Gln
50 55 60

Gly Arg Val Thr Met Thr Thr Asp Thr Ser Thr Ser Thr Ala Tyr Met
65 70 75 80

Glu Leu Arg Ser Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys Ala
85 90 95

Arg

<210> SEQ ID NO 253
<211> LENGTH: 98
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 253

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30

Ala Met His Trp Val Arg Gln Ala Pro Gly Gln Arg Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Ala Gly Asn Gly Asn Thr Lys Tyr Ser Gln Lys Phe
50 55 60

Gln Gly Arg Val Thr Ile Thr Arg Asp Thr Ser Ala Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg

<210> SEQ ID NO 254
<211> LENGTH: 98
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 254

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Ala Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

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Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys

<210> SEQ ID NO 255
<211> LENGTH: 118
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 255

Glu Val Gln Leu Val Gln Ser Gly Ser Glu Val Arg Arg Pro Gly Ser
1 5 10 15

Ser Val Arg Val Ser Cys Thr Ala Ser Gly Asp Thr Ser Ser Ser Phe
20 25 30

Thr Val Asn Trp Leu Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Gly Ile Thr Pro Met Phe Gly Thr Ala Asn Tyr Ala Gln Met Phe
50 55 60

Glu Asp Arg Val Thr Ile Thr Ala Asp Glu Met Glu Leu Ser Gly Leu
65 70 75 80

Thr Ser Glu Asp Thr Ala Val Tyr Phe Cys Ala Thr Gly Pro Ser Asp
85 90 95

Tyr Val Trp Gly Ser Tyr Arg Phe Leu Asp Thr Trp Gly Arg Gly Thr
100 105 110

Thr Val Thr Val Ser Ser
115

<210> SEQ ID NO 256
<211> LENGTH: 101
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 256

Gln Val Gln Leu Gln Gln Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Ile Ser Gly Asp Ser Val Ser Ser Asn
20 25 30

Ser Ala Ala Trp Asn Trp Ile Arg Gln Ser Pro Ser Arg Gly Leu Glu
35 40 45

Trp Leu Gly Arg Thr Tyr Tyr Arg Ser Lys Trp Tyr Asn Asp Tyr Ala
50 55 60

Val Ser Val Lys Ser Arg Ile Thr Ile Asn Pro Asp Thr Ser Lys Asn
65 70 75 80

Gln Phe Ser Leu Gln Leu Asn Ser Val Thr Pro Glu Asp Thr Ala Val
85 90 95

Tyr Tyr Cys Ala Arg
100

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<210> SEQ ID NO 257
<211> LENGTH: 98
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 257

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Glu
1 5 10 15

Ser Leu Lys Ile Ser Cys Lys Gly Ser Gly Tyr Ser Phe Thr Ser Tyr
20 25 30

Trp Ile Gly Trp Val Arg Gln Met Pro Gly Lys Gly Leu Glu Trp Met
35 40 45

Gly Ile Ile Tyr Pro Gly Asp Ser Asp Thr Arg Tyr Ser Pro Ser Phe
50 55 60

Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Ile Ser Thr Ala Tyr
65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg

<210> SEQ ID NO 258
<211> LENGTH: 98
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 258

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gly
1 5 10 15

Thr Leu Ser Leu Thr Cys Ala Val Ser Gly Gly Ser Ile Ser Ser Ser
20 25 30

Asn Trp Trp Ser Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp
35 40 45

Ile Gly Glu Ile Tyr His Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu
50 55 60

Lys Ser Arg Val Thr Ile Ser Val Asp Lys Ser Lys Asn Gln Phe Ser
65 70 75 80

Leu Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg

<210> SEQ ID NO 259
<211> LENGTH: 98
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 259

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly

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1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20                  25                  30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35                  40                  45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85                  90                  95

Ala Arg


<210> SEQ ID NO 260
<211> LENGTH: 98
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 260

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20                  25                  30

Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35                  40                  45

Ser Tyr Ile Ser Ser Ser Ser Ser Thr Ile Tyr Tyr Ala Asp Ser Val
50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Val Tyr Tyr Cys
85                  90                  95

Ala Arg


<210> SEQ ID NO 261
<211> LENGTH: 98
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
      Syntheticpolypeptide"

<400> SEQUENCE: 261

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1               5                   10                  15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20                  25                  30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35                  40                  45

Ala Val Ile Trp Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50                  55                  60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
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-continued

65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg

<210> SEQ ID NO 262
<211> LENGTH: 98
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 262

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Lys

<210> SEQ ID NO 263
<211> LENGTH: 98
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 263

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Gly Tyr
20 25 30

Tyr Met His Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met
35 40 45

Gly Trp Ile Asn Pro Asn Ser Gly Gly Thr Asn Tyr Ala Gln Lys Phe
50 55 60

Gln Gly Trp Val Thr Met Thr Arg Asp Thr Ser Ile Ser Thr Ala Tyr
65 70 75 80

Met Glu Leu Ser Arg Leu Arg Ser Asp Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg

<210> SEQ ID NO 264
<211> LENGTH: 92
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence

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<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 264

Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45

Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn
85 90

<210> SEQ ID NO 265
<211> LENGTH: 93
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 265

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Ser Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp
85 90

<210> SEQ ID NO 266
<211> LENGTH: 112
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 266

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Thr Val Asn Trp Tyr Gln Arg Leu Pro Gly Ala Ala Pro Gln Leu Leu
35 40 45

-continued

Ile Tyr Asn Asn Asp Gln Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Gly Ser Leu Val Ile Ser Gly Leu Gln
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ser Trp Asp Asp Ser Leu
85 90 95

Asn Gly Arg Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu Gly Ala
100 105 110

<210> SEQ ID NO 267
<211> LENGTH: 94
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 267

Gln Thr Val Val Thr Gln Glu Pro Ser Phe Ser Val Ser Pro Gly Gly
1 5 10 15

Thr Val Thr Leu Thr Cys Gly Leu Ser Ser Gly Ser Val Ser Thr Ser
20 25 30

Tyr Tyr Pro Ser Trp Tyr Gln Gln Thr Pro Gly Gln Ala Pro Arg Thr
35 40 45

Leu Ile Tyr Ser Thr Asn Thr Arg Ser Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Ile Leu Gly Asn Lys Ala Ala Leu Thr Ile Thr Gly Ala
65 70 75 80

Gln Ala Asp Asp Glu Ser Asp Tyr Tyr Cys Val Leu Tyr Met
85 90

<210> SEQ ID NO 268
<211> LENGTH: 93
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 268

Asn Phe Met Leu Thr Gln Pro His Ser Val Ser Glu Ser Pro Gly Lys
1 5 10 15

Thr Val Thr Ile Ser Cys Thr Arg Ser Ser Gly Ser Ile Ala Ser Asn
20 25 30

Tyr Val Gln Trp Tyr Gln Gln Arg Pro Gly Ser Ser Pro Thr Thr Val
35 40 45

Ile Tyr Glu Asp Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Ile Asp Ser Asn Ser Ala Ser Leu Thr Ile Ser Gly Leu Lys
65 70 75 80

Thr Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp
85 90

<210> SEQ ID NO 269
<211> LENGTH: 91
<212> TYPE: PRT

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<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 269

Ser Ser Glu Leu Thr Gln Asp Pro Ala Val Ser Val Ala Leu Gly Gln
1 5 10 15

Thr Val Arg Ile Thr Cys Gln Gly Asp Ser Leu Arg Ser Tyr Tyr Ala
20 25 30

Ser Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Ile Tyr
35 40 45

Gly Lys Asn Asn Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser Gly Ser
50 55 60

Ser Ser Gly Asn Thr Ala Ser Leu Thr Ile Thr Gly Ala Gln Ala Glu
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Arg Asp
85 90

<210> SEQ ID NO 270
<211> LENGTH: 91
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 270

Ser Tyr Val Leu Thr Gln Pro Pro Ser Val Ser Val Ala Pro Gly Gln
1 5 10 15

Thr Ala Arg Ile Thr Cys Gly Gly Asn Asn Ile Gly Ser Lys Ser Val
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Leu Val Val Tyr
35 40 45

Asp Asp Ser Asp Arg Pro Ser Gly Ile Pro Glu Arg Phe Ser Gly Ser
50 55 60

Asn Ser Gly Asn Thr Ala Thr Leu Thr Ile Ser Arg Val Glu Ala Gly
65 70 75 80

Asp Glu Ala Asp Tyr Tyr Cys Gln Val Trp Asp
85 90

<210> SEQ ID NO 271
<211> LENGTH: 94
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 271

Gln Ser Ala Leu Thr Gln Pro Ala Ser Val Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Ile Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

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Met Ile Tyr Glu Val Ser Asn Arg Pro Ser Gly Val Ser Asn Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Thr
85 90

<210> SEQ ID NO 272
<211> LENGTH: 94
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 272

Gln Ser Ala Leu Thr Gln Pro Pro Ser Ala Ser Gly Ser Pro Gly Gln
1 5 10 15

Ser Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asp Val Gly Gly Tyr
20 25 30

Asn Tyr Val Ser Trp Tyr Gln Gln His Pro Gly Lys Ala Pro Lys Leu
35 40 45

Met Ile Tyr Glu Val Ser Lys Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Val Ser Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Ser Ser Tyr Ala
85 90

<210> SEQ ID NO 273
<211> LENGTH: 94
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 273

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly
20 25 30

Tyr Asp Val His Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu
35 40 45

Leu Ile Tyr Gly Asn Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
50 55 60

Ser Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp
85 90

<210> SEQ ID NO 274
<211> LENGTH: 93
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:

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<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 274

Gln Ser Val Leu Thr Gln Pro Pro Ser Val Ser Ala Ala Pro Gly Gln
1 5 10 15

Lys Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Asn Asn
20 25 30

Tyr Val Ser Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Asp Asn Asn Lys Arg Pro Ser Gly Ile Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Thr Leu Gly Ile Thr Gly Leu Gln
65 70 75 80

Thr Gly Asp Glu Ala Asp Tyr Tyr Cys Gly Thr Trp Asp
85 90

<210> SEQ ID NO 275
<211> LENGTH: 93
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Syntheticpolypeptide"

<400> SEQUENCE: 275

Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

Arg Val Thr Ile Ser Cys Ser Gly Ser Ser Ser Asn Ile Gly Ser Asn
20 25 30

Tyr Val Tyr Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
35 40 45

Ile Tyr Arg Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
50 55 60

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Arg
65 70 75 80

Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp
85 90

<210> SEQ ID NO 276
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial Sequence
<220> FEATURE:
<221> NAME/KEY: source
<223> OTHER INFORMATION: /note="Description of Artificial Sequence:
Synthetic6xHis tag"

<400> SEQUENCE: 276

His His His His His His
1 5

1. A binding protein that specifically binds ErbB2, wherein the binding protein is an ErbB2 agonist.

2. The binding protein of claim **1** which reduces cellular proliferation in an ErbB2-expressing cancer cell.

3. The binding protein of claim **1** which increases apoptosis in an ErbB2-expressing tumor.

4. The binding protein of claim **1** which reduces the growth of an ErbB2-expressing tumor.

5. The binding protein of claim **2** wherein the ErbB2-expressing cancer cell is a breast cancer cell.

6. The binding protein of claim **2** wherein the ErbB2 expressing cancer cell is from a cell line selected from the group consisting of: SKBR3, BT474, MDA-MB-453 and MDA-MB-361.

7. A binding protein that specifically binds ErbB2, wherein the binding protein preferentially binds an ErbB2 extracellular domain (ECD) homo-dimer over ErbB2 ECD monomer and shed ErbB2 ECD.

8. The binding protein of claim **1**, wherein the binding protein preferentially binds an ErbB2 extracellular domain (ECD) homo-dimer over ErbB2 ECD monomer and shed ErbB2 ECD.

9. The binding protein of claim **2**, that possesses one or more or the following properties:

(a) increases ErbB2 phosphorylation in a breast cancer cell;

(b) increases the phosphorylation of one or more of AKT, MAPK and ERK; or

(c) binds ErbB2 ECD in the CR2 domain.

10. The binding protein of claim **1** which is an antibody, an antigen-binding fragment of an antibody or a small modular immunopharmaceutical (SMIP).

11. The binding protein of claim **10** which is an antigen-binding fragment of an antibody, wherein the antigen-binding fragment is selected from the group consisting of: a Fab fragment, an F(ab')2 fragment, an scFv, a dAb, and Fv fragment and a VHH.

12. The binding protein of claim **1**, which is human antibody or an antigen-binding fragment thereof.

13. The binding protein of claim **1**, wherein the ErbB2 is human ErbB2 (SEQ ID NO: 246).

14. A binding protein that specifically binds ErbB2, wherein the binding protein comprises:

(a) a VH domain comprising the CDR1, CDR2 and CDR3 amino acid sequences set forth in any one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 65 or 67; or

(b) a VL domain comprising the CDR1, CDR2 and CDR3 amino acid sequences set forth in any one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 63, 64, 66, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94 or 95; or

(c) a VH of (a) and a VL of (b).

15. The binding protein of claim **14**, comprising the VH CDR1, CDR2 and CDR3 amino acid sequences and the VL CDR1, CDR2 and CDR3 sequences of any one of: S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_1E1, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, S1R3C1_CS_1B10, S1R3A1_BMV_1F3, S1R3B1_BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11, S1R3B1_BMV_1A10, S1R3A1_CS_1D11, S1R3C1_DP47_1H1, S1R3A1_CS_1B12, S1R3B1_BMV_1H5, S1R3A1_DP47_1A6, S1R3B1_DP47_1E1 or S1R3B1_BMV_1A1.

16. A binding protein that specifically binds ErbB2, wherein the binding protein comprises:

(a) a VH having the amino acid sequence that is at least 90% identical to any one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 65 or 67; or

(b) a VL having the amino acid sequence that is at least 90% identical to any one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 63, 64, 66, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94 or 95;

(c) a VH of (a) and a VL of (b); or

(d) a VH and a VL amino acid sequence that are at least 90% identical to the VH and VL, amino acid sequences, respectively, in any one of S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_1E1, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_1A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, S1R3C1_CS_1B10, S1R3A1_BMV_1F3, S1R3B1_BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11, S1R3B1_BMV_1A10, S1R3A1_CS_1D11, S1R3C1_DP47_1H1, S1R3A1_CS_1B12, S1R3B1_BMV_1H5, S1R3A1_DP47_1A6, S1R3B1_DP47_1E1 or S1R3B1_BMV_1A1.

17. The binding protein of claim **16**, wherein the binding protein comprises:

(a) a VH having the amino acid sequence that is at least 95% identical to any one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 65 or 67; or

(b) a VL having the amino acid sequence that is at least 95% identical to any one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 63, 64, 66, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94 and 95; or

(c) a VH of (a) and a VL of (b); or

(d) a VH and a VL amino acid sequence that are at least 95% identical to the VH and VL, amino acid sequences, respectively, in any one of S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_1E1, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_1A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, S1R3C1_CS_1B10, S1R3A1_BMV_1F3, S1R3B1_BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11, S1R3B1_BMV_1A10, S1R3A1_CS_1D11, S1R3C1_DP47_1H1, S1R3A1_CS_1B12, S1R3B1_

BMV_1H5, S1R3A1_DP47_1A6, S1R3B1_DP47_1E1 or S1R3B1_BMV_1A1.

18. The binding protein of claim **16**, wherein the binding protein comprises:

(a) a VH having the amino acid sequence of any one of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 65 or 67; or

(b) a VL having the amino acid sequence of any one of SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 63, 64, 66, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94 or 95; or

(c) a VH of (a) and a VL of (b); or

(d) a VH and a VL amino acid sequence of the VH and VL, amino acid sequences, respectively, in any one of S1R2A_CS_1F7, S1R2A_CS_1D11, S1R2C_CS_1D3, S1R2C_CS_1H12, S1R2A_CS_1D3, S1R3B2_BMV_μl, S1R3C1_CS_1D3, S1R3B2_DP47_1E8, S1R3B2_BMV_1G2, S1R3B2_BMV_1H5, S1R3C1_CS_1A6, S1R3B2_DP47_1C9, S1R3B2_DP47_1E10, S1R3C1_CS_1B10, S1R3A1_BMV_1F3, S1R3B1_BMV_1G11, S1R3A1_BMV_1G4, S1R3B1_BMV_1H11, S1R3A1_CS_1B9, S1R3B1_BMV_1H9, S1R3A1_CS_1B10, S1R3B1_BMV_1C12, S1R3C1_BMV_1H11, S1R3B1_BMV_1A10, S1R3A1_CS_1D11, S1R3C1_DP47_1H1, S1R3A1_CS_1B12, S1R3B1_BMV_1H5, S1R3A1_DP47_1A6, S1R3B1_DP47_1E1 or S1R3B1_BMV_1A1.

19. The binding protein of claim **14** or claim **16**, which is a SMIP.

20. A SMIP comprising an amino acid sequence that is at least 90% identical to the amino acid sequence of any one of SEQ ID NOS: 159, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231 or 233, excluding the leader sequence.

21. The SMIP of claim **20**, comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of any one of SEQ ID NOS: 159, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231 or 233, excluding the leader sequence.

22. The SMIP of claim **20**, comprising the amino acid sequence of any one of SEQ ID NOS: 159, 173, 175, 177, 179, 181, 183, 185, 187, 189, 191, 193, 195, 197, 199, 201, 203, 205, 207, 209, 211, 213, 215, 217, 219, 221, 223, 225, 227, 229, 231 or 233, excluding the leader sequence.

23. A nucleic acid molecule encoding the SMIP of claim **20**.

24. A nucleic acid molecule that encodes a binding protein that specifically binds ErbB2, wherein the nucleic acid molecule comprises a nucleotide sequence selected from:

(a) the nucleotide sequence of any one of SEQ ID NOS: 96, 98, 100, 102, 104, 106, 108, 110, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, 152, 154 or 156; or

(b) the nucleotide sequence of any one of SEQ ID NOS: 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, 127, 129, 131, 133, 135, 137, 139, 141, 143, 145, 147, 149, 151, 153, 155 or 157; or

(c) both the nucleotide sequence of (a) and the nucleotide sequence of (b).

25. The nucleic acid molecule of claim **24**, comprising the nucleotide sequence of any one of SEQ ID NOS: 158, 172, 174, 176, 178, 180, 182, 184, 186, 188, 190, 192, 194, 196, 198, 200, 202, 204, 206, 208, 210, 212, 214, 216, 218, 220, 222, 224, 226, 228, 230 or 232.

26. A composition comprising the SMIP of claim **20**.

27. The composition of claim **26**, further comprising an additional therapeutic or diagnostic agent.

28. The composition of claim **27** that comprises an additional therapeutic agent, wherein the therapeutic agent is a chemotherapeutic or anti-inflammatory agent.

29. A host cell comprising a nucleic acid molecule of claim **24**.

30. The host cell of claim **29**, selected from the group consisting of an HEK cell, an NS0 cell and a CHO cell.

31. A method for producing a binding molecule that specifically binds ErbB2, or a SMIP that specifically binds ErbB2, comprising the step of culturing the host cell of claim **29** under conditions the permit protein expression.

32. A method for reducing ErbB2-mediated proliferation of a cancer cell comprising the step of administering to a subject or mammal in need thereof an effective amount of a composition of claim **26**.

33. A method for reducing tumor growth of an ErbB2-expressing tumor, comprising administering to a subject or mammal in need thereof an effective amount a composition of claim **26**.

34. A method for increasing apoptosis in an ErbB2-expressing tumor, comprising administering to a subject or mammal in need thereof an effective amount of a composition of claim **26**.

35. The binding protein of claim **1**, which is detectably labeled.

36. A method for detecting an ErbB2 expressing tumor in a subject, comprising administering the binding protein of claim **35**.

37. A method for detecting ErbB2 in a sample from a subject comprising the step of contacting the sample with a binding protein of claim **14** or **16**, or a SMIP of claim **20** under conditions that permit binding and detecting binding, wherein binding indicates the presence of ErbB2.

38. A method of treating cancer characterized by ErbB2 expression comprising administering to a mammal or subject in need thereof an effective amount of a binding protein of claim **1**.

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